OLUME 22 January, 1956

THE AMERICAN SURGEON

PUBLISHED MONTHLY BY
THE WILLIAMS & WILKINS COMPANY
BALTIMORE 2, MARYLAND

Entered at the Post Office in Baltimore, Maryland as second-class matter.
Subscription price $10.00

CONTENTS, JANUARY

THIS ISSUE IS PUBLISHED IN MEMORY OF DOCTOR THOMAS G. ORR, EDITOR

The American Surgeon

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Subscription price is $10.00 per volume. In countries outside the United States, except Canada, add $1.25 per volume postage. Canadian postage: add $.50 per volume. Single copies, when available, are $1.00, plus $.25 postage outside the U. S.

Publisher

THE WILLIAMS & WILKINS CO.

Mt. Royal & Guilford Aves., Baltimore 2, Md.

THE
AMERICAN SURGEON

Vol. 22, No. 1 January, 1956

ANNOUNCEMENT

This issue of The American Surgeon is published in memory of Doctor Thomas G. Orr, Emeritus Professor of Surgery, University of Kansas.

The material for the issue has been furnished by associates of Doctor Orr on the Faculty of the University of Kansas School of Medicine, and by his former Residents, Interns and Students.

TRIBUTE TO DR. ORR

Youth is the period of day dreams and dreams of the future. Only a very few realize their youthful dreams, and of them only a minute fraction exceed those early ambitions. Thomas Grover Orr belongs to this minute fraction. When I first knew him during our student days in Baltimore, he told me that he had two ambitions—one to be a surgeon, the other to practise in Kansas City. If I had gazed into a crystal ball at that time and told him that he would be not only a surgeon and practise in Kansas City but also would be professor and chairman of the department of surgery at the University of Kansas; president of the Kansas City Academy of Medicine, the Kansas City Surgical Society, the Southwest Clinical Society, the Missouri Valley Medical Society, the Western Surgical Association, the American Surgical Association; the Southwestern Surgical Congress; receive the honorary degree of Doctor of Science from his Alma Mater the University of Missouri—with membership in Alpha Omega Alpha and Sigma Xi thrown in for good measure—I am sure he would have spoken most disrespectfully of all prognosticators and prophets.

For a great many years, Dr. Orr's path and my path frequently have crossed but more commonly run alongside each other. We were in the same class at Johns Hopkins; belonged to the same medical fraternity, into which we were

initiated the same night; and attended the same classes and clinics. After graduation, our paths diverged for some five years, then drew together again in 1914, and, with the exception of some two or three years, have since run side by side. For 25 years, he was chairman of the department of surgery while I was his colleague, occupying the same post in the department of medicine. So I have known him through fair weather and stormy weather; through warm sunshiny days as well as through bleak chilly ones. Fair weather has not seduced him nor stormy weather terrified him; warm days have not enervated him nor chilly ones dampened his enthusiasm. Through all these years, he has pursued his course, calmly, unruffled, and unhurried with his goal constantly before his eyes, at first perhaps dim in the distance but in later years becoming clearer and closer. His goal--to be worthy as a surgeon of the heritage of the past and to pass on this heritage to his successors.

Physicians and surgeons have been described as belonging to one of three groups—those who look on their profession solely as a business; those who see in it only an experimental science; and those who regard it as a mission. Dr. Orr certainly never viewed his profession as a business, and, although his important scientific investigations prove his love of surgery as a science, he never operated upon a patient just to gratify a scientific curiosity or to obtain a remarkable pathologic specimen. Surgery always has been for him a mission, whose first challenge is to heal.

Dr. Orr has made many important contributions to surgery, yet he does not belong to those who think that all progress which has been made in surgery during the last few years is the result of research. He is a deep student of the history of surgery and is fond of quoting the words of Guy de Chauliac, the great medieval surgeon: "We are only children on the neck of a giant." His lectures on the history of surgery are most popular and well attended by the medical students.

Dr. Orr has had a distinguished career as surgeon, investigator and teacher. Generations of surgical residents have learned their skill from him. He is respected by his colleagues; revered by his students; beloved by his patients.

RALPH H. MAJOR, M.D.
University of Kansas
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Thomas G. Orr, M.D.

May 9, 1884–November 19, 1955

SURGICAL TREATMENT OF DIVERTICULITIS OF THE COLON

CLAUDE F. DIXON, M.D.

Rochester, Minn.

Diverticulitis of the sigmoid colon was not fully recognized as a distinct disease entity amenable to surgical treatment until the turn of the century. During the last 50 years an increasing number of reports has led to a keener appreciation of the pathologic variations of this disease. Yet with these well-documented studies and the increasing experience of numerous surgeons, definitive treatment of diverticulitis of the sigmoid colon still is quite variable and offers many interesting individualized problems of attack.

In 1904 an important publication was written by Beer,[1] the first significant treatise appearing in American literature. In this article 18 cases of diverticulitis reported in the literature were grouped, and a compilation of the variations of diverticulitis was made. Although the cases were few in number, there is little to be added to Beer's adequate description of this disease. He grouped the cases as follows:

1. Diverticulitis which produces stenosis of the sigmoid or the upper part of the rectum: 6 cases reported, 1 with abscess, 2 with sigmoidovesical fistula, and 1 with mesenteric abscess.
2. Diverticulitis which leads to perforation into the peritoneum: 5 cases.
3. Diverticulitis which leads to abscess or localized peritonitis in the left iliac fossa: 2 cases.
4. Diverticulitis which perforates into the urinary bladder or causes dense adhesions about the bladder ("This suggests the gravest of disease and is an inoperable condition"): 4 cases.
5. Diverticulitis causing mesenteritis: found in most of the cases studied.
6. Diverticulitis associated with appendicitis: rare.
7. Diverticulitis associated with carcinoma: 1 instance reported by Hochenegg. "The future alone can show the importance of chronic ulceration leading to carcinoma."

Among the 18 cases reported by Beer there were no colocutaneous or coloenteric fistulas, which have since been found to be a complication of diverticulitis. Also the term "*mesenteritis*" has been dropped in favor of "*peridiverticulitis*," a term introduced by Mayo, Wilson and Giffin in 1907.[8] Not only was Beer's discussion of pathology complete, but his opinions of etiology still can be considered up to date. In summarizing the theoretical and experimental data at his command, he concluded that, although the causes of diverticula are multiple, the most important factor is a muscular weakness or deficiency in the intestinal wall. This weakness allows the mucosa to herniate through to produce the sacculations. He discredited the theory of mucosal herniation through muscular slits

Assistance is acknowledged to my former assistant, Dr. Clyde A. Pitchford, Riverside, California.

channeling blood vessels, since diverticula occur in any portion of the bowel's circumference. Nevertheless, it has been observed since that almost all diverticula occur in that span of bowel between the mesentery and the longitudinal muscle. At this site the major circumferential blood vessels enter the bowel from the mesentery. Hence this theory should not be totally discarded.

Although Beer stressed muscular weakness as the primary cause of diverticula, he still mentioned diet, obesity and intracolonic pressure as etiologic factors. Of significance are the recent studies of Carlson and Hoelzel[3] who suggest that fat deposits along the mesenteric border afford weak spots in the colon in which diverticula can develop. Although experimenting with rats, they found that the incidence of diverticula was influenced greatly by a diet that formed a hard constipated stool. The muscular spasm of the bowel necessary to initiate propulsion of the hard fecal contents was thought sufficient to produce the mucosal herniations through this weaker part. The diverticula were found to occur along the mesenteric border of the colon and in the epiploica; this portion of the bowel has the greatest content of fat.

I believe it can be stated that the cause of diverticula in the colon is multiple. It is generally agreed that the herniations are acquired, or false, diverticula for the most part. Muscular weakness, vascular channels, diet, obesity and possibly an inherent predisposition all influence their development. They are not so clear-cut as diverticula of the bladder where obvious mechanical factors such as obstruction, dilatation and intraluminal pressure are generally assumed to be the direct cause. Likewise, the cause of colonic diverticula is not so obvious as the cause of epigastric hernias wherein vascular channels splitting the tough linea alba complete the pathogenesis without much doubt.

INCIDENCE

As evidenced by the meager number of case reports of diverticulitis prior to the early nineteen hundred's, the reported incidence of this disease has certainly increased. This undoubtedly has paralleled the general increase in the population of the older age group. Diverticulosis and diverticulitis are diseases of aging, as it is rare to discover their onset prior to the age of 40. The incidence of diverticulosis was found to be about 5 per cent in a study of 24,620 roentgenograms of the colon made at the Mayo Clinic.[11] In more than two-thirds of the patients the diverticula are demonstrable not only in the sigmoid colon but also in other parts of the large bowel as well. Twenty-eight per cent are found to be localized to the sigmoid colon alone. The incidence of diverticulitis in those patients with demonstrable diverticulosis is about 15 per cent. Surgical measures are necessary for the treatment of diverticulitis in just one-fourth of the patients, however. In other words, less than 4 per cent of patients with diverticulosis require surgical treatment.

SYMPTOMS

The most common symptom of diverticulitis, namely, abdominal tenderness with or without the generalized symptoms of fever and malaise, is the direct

result of infection. The tenderness and pain are in direct relationship to the acuteness of the process and, as pointed out in earlier articles, may resemble *"left-sided appendicitis."* Constipation is a frequently occurring symptom, and may be associated with alternating diarrhea, especially if stenosis of the colon exists.

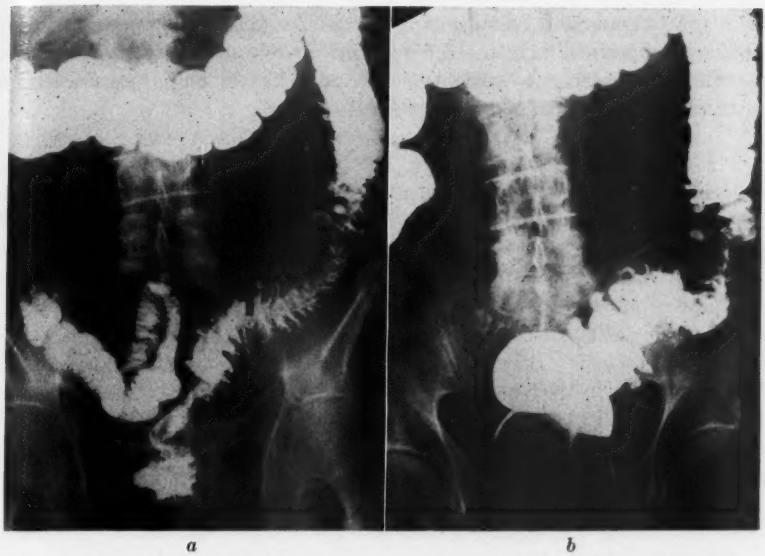
The presence of blood in the stool is not a rare complaint, being found in about 10 per cent of the patients.[10, 11] There was a history of bleeding in 20 per cent of the patients in 274 cases of diverticulitis studied by Morhous[9], but blood was demonstrable by laboratory tests in only 5 per cent. Whenever this symptom is present, the coexistence of carcinoma should be ruled out. That this is not easily done is reflected in the report of Scarborough and Klein[13] who found polyps in patients in 16 cases of rectal bleeding supposedly due to diverticulitis. In 4 of these patients the polyps had undergone malignant changes necessitating resection. In some of the earlier reports of diverticulitis a high incidence of associated carcinoma was mentioned.[6, 15] Hence it was generally accepted that there was a direct relationship between the two diseases. Subsequent observers, however, disproved this linkage. Rankin and Brown[11] found only 4 cases of carcinoma in 227 cases of diverticulitis. Similarly Rowe and Kollmar[12] found carcinoma in only 2.2 per cent of the cases of diverticulitis. Most patients with rectal bleeding apparently due to diverticulitis should have resections to avert the possibility of overlooking a masked carcinoma. The following case illustrates this point.

Case 1. A man aged 70 had been examined at intervals since 1927 when he had undergone cholecystectomy for gallstones. In 1937 a diagnosis of pernicious anemia had been made and on that account his condition had been reviewed every two years. In May 1951, he noticed that his bowel movements were ribbon-like. There was no associated pain, blood or change in bowel habits. Roentgenographic studies at that time revealed diverticulitis of the sigmoid colon with diverticulosis of the remaining part of the colon (fig. 1*a*). Medical therapy was prescribed.

In December 1951, he had a sudden movement of blood, followed later by passage of blood clots. Subsequently he came to the Mayo Clinic where an examination revealed an irregular fixed mass in the left lower quadrant of the abdomen. The rectal examination gave negative results. Roentgenographic study depicted narrowing of a fairly long segment of the colon in the region of the juncture of the descending colon and sigmoid (fig. 1*b*). This had the appearance of subacute and chronic diverticulitis. Because of the bleeding, resection was recommended to rule out the presence of a carcinoma. Thereupon segmental resection of the sigmoid colon was performed, with proximal loop transverse colostomy. The pathologic diagnosis was diverticulosis and peridiverticulitis. In the midportion of the resected specimen there was a 10 cm. segment in which the bowel was thickened, the lumen narrowed and the mucosal folds edematous and hemorrhagic.

The postoperative course was complicated by prostatic obstruction which necessitated transurethral prostatic resection. Six weeks postoperatively the patient underwent an uneventful closure of the colonic stoma.

That the course of the pathologic changes in the colon following the effects of diverticulitis dictates the symptoms is obvious. Obstructive symptoms occur in about one-third of the patients and fistula in 42 per cent.[10] Fistulas penetrate the abdominal wall about as frequently as they penetrate the bladder. The usual and diagnostic symptom of vesicosigmoidal fistula is pneumaturia. Other leading symptoms of this condition are the passing of feces in the urine, dysuria, fre-



a *b*

FIG. 1*a*. Diverticulitis of the sigmoid colon with diverticulosis of the remaining colon. *b*. Narrowing of a fairly long segment of colon in the region of juncture of the descending and sigmoid colon.

quency and even hematuria.[7] These fistulous tracts may be very small and difficult to demonstrate by cystoscopy. The demonstration of barium in the bladder when a barium enema is given will aid in confirming the diagnosis.

Coloenteric fistulas are not common. When they occur, the patient may give a history of having passed pus by rectum. The preoperative diagnosis of such a fistula is apt to be missed and the condition found at the time of exploration. The symptoms of this condition are generally due to the primary sigmoidal diverticulitis.

DIAGNOSIS

Although the symptoms and signs of diverticulitis are useful adjuncts to diagnosis, reliance is placed primarily upon study of the colon with a barium enema. Proctoscopic examination is advantageous as a complementary measure, and can be of great help in the diagnosis of a coexisting carcinoma. Proctoscopic findings compatible with diverticulitis include visible diverticula, or sacculation of the sigmoid. There is abnormal tenderness with limited mobility of the bowel. The rectosigmoid is more sharply angulated than usual.

Diverticulitis of the colon is characterized roentgenoscopically by spasticity of the bowel with saw-toothed edges. The edema produces a cone-shaped filling defect, tapering off at the edges (fig. 1*a* and *b*). The disease involves a relatively long segment of the colon as compared to a carcinoma, and there is preservation of the mucosal folds.

Both proctoscopic and roentgenoscopic examinations should be made of each patient with diverticulitis of the colon so that there may be accord in the diagnosis. These studies, carried out with an adequate history and physical examination, lead to the diagnosis in practically all cases.

TREATMENT

Historic Aspects. Numerous excellent articles in the literature have given a better understanding of the pathology and treatment of diverticulitis of the sigmoid colon. It is beyond the scope of this paper to review all these significant papers and studies. Instead, I have found it relevant to review three Mayo Clinic papers published in 1907, 1930 and 1947 respectively. In so doing a historic picture can be drawn of the surgical treatment of diverticulitis at this institution.

The first paper, in 1907, by Mayo and co-workers[8] presented 5 proved cases of diverticulitis and 4 probable cases. The 5 proved cases were characterized clinically by a mass in the left lower quadrant and in 1 case there was obstruction in addition. In 2 of the cases there were signs and symptoms of "*left-sided appendicitis.*" Because of the abdominal tumor, exploration and primary resection were carried out. Two of the 5 patients died postoperatively of peritonitis. A complete description of the pathologic findings was given, and the term "*peridiverticulitis*" was introduced to describe the chronic inflammation of the subserosa about the diverticula. They mentioned how difficult it was to differentiate the disease grossly from carcinoma of the colon. In conclusion, they advocated the following surgical treatment of diverticulitis:

1. If an abscess is present, simple incision and drainage should be carried out.
2. If obstruction has developed, a colonic stoma should be made proximal to the lesion, followed by resection at a later date.
3. If a tumor is present which subsequently subsides, it is better to do a primary resection prior to the development of abscess and fistula.

In the succeeding years, however, with improved preoperative diagnosis, the primary resection used for carcinoma was abandoned because of the high operative mortality associated with it. Instead, proximal colostomy was performed to put the diseased bowel to rest and to adjust the surgical intervention according to the therapeutic response of the patient.

The next paper, which represented the period 1923 to 1925, was written by Rankin and Brown[11]. They reported on a group of 227 patients, 48 of whom underwent surgical treatment. The indications they listed for surgical therapy included acute perforation (rare), abscess formation, fistula, obstruction and inability to rule out carcinoma. The operative procedure advocated was a three stage resection, initiated by preliminary transverse colostomy, to be followed by sigmoidectomy, and later closure of the colonic stoma. They indicated that the preliminary colonic stoma should be left intact for about a year before further surgical steps are taken. Occasionally, complete recession of the disease was seen, thus obviating resection. In their group of 48 patients there were 5 postoperative deaths, an incidence of about 10 per cent.

The third paper, which represented a five year period, was published in 1947 by Pemberton and co-workers[10]. In this study the number of surgically treated patients had trebled, totalling 144. An excellent analysis of the surgical treatment given at the Mayo Clinic since 1908 was made. The following operative procedures with their results were described:

1. Local excision of a diverticulum or fistula. This was carried out in 17 patients and it was rare to find the inflammatory reaction so limited that this could be done. Nine patients had good results, however, and 5 had recurrence of the disease.

2. Colostomy as a preliminary procedure for resection in stages or as a temporary measure to allow healing of the diseased colon. Earlier, 31 patients underwent closure of the colonic stoma with the supposition that the diverticulitis had healed. Of these 31 patients, only 9 remained well. Twenty patients had recurrent disease.

3. Resection of the diseased colon, preceded by colostomy, was advocated as the procedure of choice. This was accompanied by the lowest operative mortality and morbidity, and was employed in 41 patients with no deaths. It was advised that the colonic stoma should be present six months to a year prior to resection. Should there be a question of coexisting cancer, the resection should follow colostomy as soon as feasible. The operative procedure of choice under these circumstances would be exteriorization, rather than anterior resection.

4. Primary resection had been done in 48 patients during the period 1941 to 1945. This was done as an exteriorization procedure in 38 of the 48 patients. Anterior resection was done with concomitant colostomy in 6 instances, and without colostomy in 4 instances. In the entire group there were 2 deaths, giving an operative mortality rate of about 4 per cent.

The conclusions of this report were that primary resection with concomitant colostomy was a safe procedure, and in the severely ill patient three stage procedures were the method of choice.

Thus it can be seen that the initial surgical attack of diverticulitis was primary resection. This procedure was used earlier as the surgeons were actually diagnosing the disease preoperatively as cancer. Because of the mortality associated with this type of surgical treatment, however, operations to be performed in stages were developed. At the present time some surgeons are reverting to primary resection.[2, 14] Such a procedure has become feasible because of the aid offered by preoperative preparation; the antibiotics not only aid in sterilizing the bowel but minimize the surrounding inflammatory reaction.

Medical Management. It must be remembered that diverticulitis of the colon causes symptomatic diverticulitis necessitating surgical treatment in about 4 or 5 per cent of patients. In the majority of patients diverticulitis is a medical problem. Medical treatment has been strengthened by the use of antibiotics such as terramycin. Briefly, medical management includes a minimal-residue diet, local heat or diathermy to the abdomen, antispasmodics and antibiotics. As a general rule, strong cathartics are not administered, but a mild cathartic such as phospho-soda (Fleet) will aid in the production of a soft stool. This

drug also is used in the preparation of the colon for operation, for with its cathartic action it brings a greater concentration of terramycin into the colon. The action of antispasmodics is useful in relaxation of the associated spasm so that there will be a more efficient surface action of the antibiotics. The results of medical therapy have been gratifying, and needless to say, such treatment must be carried out to a certain extent after the patient leaves the hospital.

Surgical Therapy. Acute Phase. The acute complications of diverticulitis are perforation, abscess, obstruction and peridiverticulitis. Acute perforation in diverticulitis of the sigmoid colon is a difficult diagnosis to make preoperatively. It is not a common complication of diverticulitis as the infective process usually is slow enough to produce localization and abscess formation. Consequently, with free perforation there will be no localizing signs and the patient presents with diffuse peritonitis. Direct surgical treatment of the perforation such as primary closure or primary resection is not advised because of the overwhelming infection which is present. The perforation can possibly be sealed with an epiploic tag if there is not excessive peridiverticulitis. The recommended procedure, however, is transverse colostomy with drainage of the involved part. After a period of two to four months the diseased colon can be resected and the colonic stoma closed at a later date. If there is free mobility of the mesocolon, the sigmoid can be elevated and an exteriorization operation performed in two stages. It would not be good judgment to free up the mesosigmoid in the face of peridiverticulitis extending through the mesentery, however.

With abscess formation, there has been adequate walling-off of a perforating lesion. If possible, this should be drained extraperitoneally and a proximal transverse colostomy performed. Although simple drainage of the abscess results in an occasional cure, further difficulties of the diseased sigmoid are prone to occur. Consequently, resection should be performed after subsidence of the inflammatory process. With adequate chemotherapy resection can be done, with end to end anastomosis, and the colostomy opening closed as a third stage.

Rarely, one may find rectal diverticulitis which will present as a perirectal abscess.[4] Drainage of the rectal abscess should be accompanied by transverse colostomy to facilitate ultimate healing. The colostomy opening then can be closed at a later date without further surgical therapy in the rectum. Usually, healing of rectal diverticulitis takes place slowly despite diversion of the fecal stream by transverse colostomy. These stubborn lesions persist with marked inflammatory proliferation in the perirectal space despite normal roentgen findings and normal bowel mucosa as determined by proctoscopic examination. It then is necessary to carry out prolonged treatment by warm irrigations through the distal colonic stoma, hot sitz baths, and diathermy, as well as antibiotic therapy. Only with complete resolution can closure of the colostomy opening be done with safety. One or two years may be required for treatment to become effective. Resection of the diseased rectum has not been found necessary for eventual healing.

Obstruction necessitates the employment of a three stage procedure. The proximal colostomy opening should be placed in the transverse colon in order

to obviate the difficulty caused by the presence of an inguinal colonic stoma while sigmoid resection is being performed at a later date. There is no good reason to delay resection of the sigmoid beyond an interval of six to eight weeks after transverse colostomy.

Peridiverticulitis is seen in almost all cases of diverticulitis in which other complications are present. When peridiverticulitis is seen alone, the bowel wall is thickened because of edema and fibrosis and has small abscesses scattered throughout. In this phase of the disease the infection has not been severe enough to produce a large abscess nor has the lesion progressed with time to become stenotic and obstructing. These patients can be treated adequately under the medical regimen, as mentioned previously. Terramycin in doses of 750 mg. given four times daily has improved the results of conservative treatment. Yet there are some patients who present an intractability to medical therapy. They have none of the more severe complications such as fistula, abscess or obstruction, however, but are chronically ill. Whether the illness is due to dietary indiscretion or the natural course of their disease is not known. The repeated episodes of recurrent diverticulitis may yet respond to active medical therapy. However, the likelihood not only of eventual complications but also of lost time and inconvenience makes resection of the sigmoid advisable. This group of patients tolerates resection best during a quiescent period and can be treated by primary resection with concomitant colostomy. The colonic stoma may be closed six to eight weeks postoperatively.

Chronic Complications. The chronic complications of diverticulitis consist of fistula formation and the occurrence of cancer. These are elective surgical problems and can be attacked with adequate preoperative preparation. The fistula may be coloenteric, colocutaneous, or colovesicular in type, or a combination of any two of these. These conditions are handled most satisfactorily by a three stage procedure. This is initiated by transverse colostomy followed in 6 to 12 weeks by resection of the sigmoid and fistulous tract. When there is a fistula into the bladder, suprapubic cystostomy is carried out simultaneously with repair of the bladder. The cystostomy tube can be removed 10 to 14 days postoperatively. Most colovesical fistulas are in the posterior wall of the bladder, making their repair quite simple. However, when the fistula is lower in the rectosigmoid, the communication may be in the base of the bladder. Under these circumstances the bowel must be dissected out and freed from this pelvic structure. Colovesical fistulas have not been found to heal under medical treatment.[5]

In dealing with colocutaneous fistulas it has been found advantageous to incise the abdomen in such a way as to include the fistulous tract. In this manner, the fistula will be completely removed.

Coloenteric fistulas may offer some difficulties in the operative attack, and because of several communications may present a difficult pattern to diagnose preoperatively. Because communication usually is between the small bowel and the colon, transverse colostomy may be only partially effective in resolving the infective process. Nevertheless there are some patients in whom there are sur-

prisingly few adhesions and in whom the fistulous tracts are quite discrete. One must be prepared to resect not only the colon but also the segment of small bowel involved in the fistulous tract.

In resecting the diseased sigmoid colon, a complementary loop transverse colostomy again is advised to protect the primary anastomosis. Exteriorization of the colon as for an obstructive lesion also is applicable and is an efficacious procedure as well.

When one is confronted with the problem of eliminating the possible coexistence of carcinoma superimposed on diverticulitis, surgical treatment must be direct. In this instance the suppurative process usually is not so extensive that it cannot be controlled with antibiotic therapy. The surgical approach can be made satisfactorily in two stages, employing primary resection with concomitant colostomy or an exteriorization procedure. Numerous surgeons today are advocating primary resection without proximal colostomy in the treatment of low sigmoid and rectosigmoid cancer. Despite this trend, in the presence of the inflammatory reaction from diverticulitis, proximal colostomy has proved to be a much safer procedure. Postoperative infection, peritonitis and fistula formation will be practically nonexistent with this precautionary measure.

The following cases illustrate the problems associated with the differential diagnosis of cancer and diverticulitis:

Case 2. A man aged 35 was first seen in June 1943, with a history of having had occasional bloody bowel movement during the previous six months. Three months prior to admission he had dysuria and pneumaturia. Treatment in his home community with sulfonamides had afforded only temporary relief of the urinary symptoms. However, he had continued to have pneumaturia and he had finally noticed undigested food in his urine.

Examination revealed only tenderness in the left lower quadrant of the abdomen. The results of rectal examination were negative. Proctoscopic examination disclosed perianal scarring and small polyps at a distance of 16 and 8 cm. from the anal orifice. On roentgenoscopic examination a carcinoma of the sigmoid colon was seen. A polypoid lesion about 1 cm. in diameter was situated below the carcinoma (fig. 2). At operation a large tumor involving the sigmoid and bladder was found. It was uncertain whether the tumor was inflammatory or neoplastic. The liver was not affected. A temporary loop transverse colostomy was done. In six weeks, resection of the descending, sigmoid and rectosigmoid colon was performed and end to end colorectostomy was utilized to re-establish continuity. The tumor attached to the bladder was removed, and the bladder was repaired and drained by suprapubic cystostomy. The pathologist reported that the tumor was an ulcerating adenocarcinoma, grade 1. No lymph nodes were involved by metastasis. One month postoperatively the colonic stoma was closed. The patient has been seen this year, 12 years postoperatively, and is in good health without evidence of recurrence.

Case 3. A woman aged 49 was seen in August 1942, because of chronic constipation. Alternating diarrhea and constipation had started five months previously and blood had been noticed in the stool the preceding week. She had lost only 2 or 3 pounds. Rectal examination revealed an extrarectal mass. Proctoscopic examination disclosed edema of the sigmoidal mucosa, with sacculation and occasional diverticula. The impression of the proctoscopist was that the condition was diverticulitis.

Roentgenoscopic examination of the colon revealed a perforating tumefactive lesion in the upper part of the sigmoid. There was perisigmoidal abscess formation, and several fistulous tracts led from the abscess cavity into the perisigmoidal soft tissue. There was

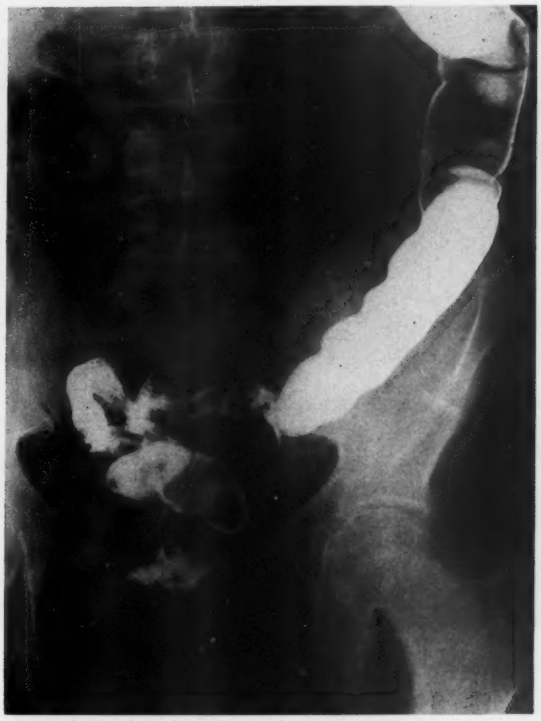
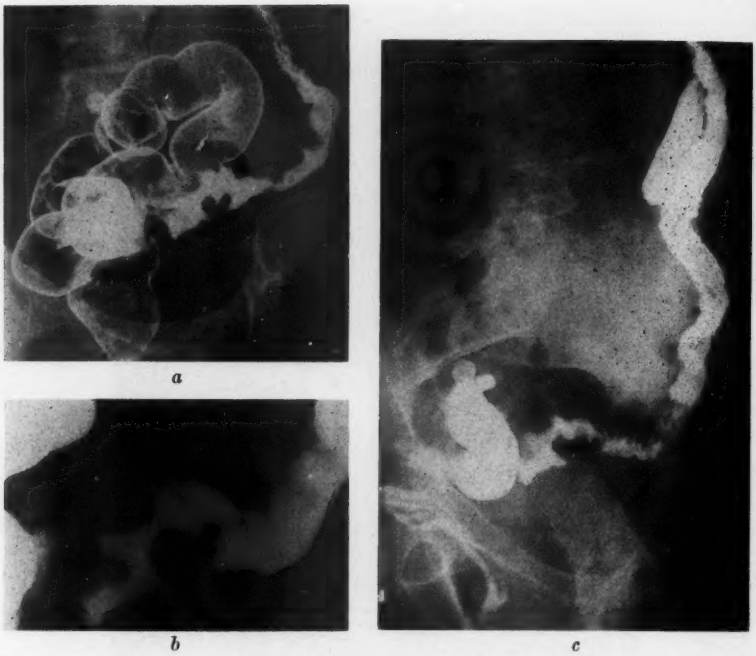


FIG. 2. Carcinoma of the sigmoid colon and a polypoid lesion about 1 cm. in diameter below the carcinoma.

no evidence that the lesion was neoplastic (fig. 3*a* and *b*). The patient was hospitalized and a strict medical regimen was instituted for the treatment of diverticulitis. In two weeks the patient had a good clinical response, and re-examination with a barium enema, advised because of persistent rectal bleeding, disclosed a perforating lesion of the sigmoid. It was the opinion of the roentgenologist at this time that the lesion was malignant (fig. 3*c*). The patient was operated upon and a perforating annular, ulcerating, infected adenocarcinoma of the sigmoid was found. This had involved the peritoneum, although the lymph nodes were uninvaded. There was associated diverticulosis. The lesion was removed by exteriorization, and in eight weeks the colonic stoma was closed. When seen again eight months later the patient had gained 14 pounds and felt better despite some pelvic pain and intermittent vaginal bleeding. Examination revealed a large movable pelvic mass. She underwent re-exploration and total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed for a metastatic adenocarcinoma involving these organs. The patient recuperated from the operation but died elsewhere four months postoperatively.

These 2 cases illustrate the difficulty of distinguishing between carcinoma and diverticulitis both preoperatively and at the time of operation. In the former case the history was compatible with diverticulosis while in the latter the necessity of correlating clinical observation with laboratory findings is emphasized.



a *b* *c*

FIG. 3*a*. A perforating lesion of the upper part of the sigmoid. There is perisigmoidal abscess formation, and several fistulous tracts lead from the abscess cavity to the perisigmoidal soft tissue. There is no positive evidence of neoplasm. *b*. Spot roentgenogram of the lesion in *a*. *c*. Roentgenogram made after two weeks of medical treatment. It was the opinion of the roentgenologist that this lesion was malignant.

SUMMARY

A brief review of the historic aspects of diverticulitis of the colon is presented along with a statement of the trends of surgical treatment of diverticulitis at the Mayo Clinic during the past 48 years. It is pointed out that diverticulosis is in general an incidental finding, occurring in about 5 per cent of the general population. Most patients with diverticulitis can be treated medically, and only 4 per cent of the patients with diverticulosis will be treated surgically.

The surgical treatment of diverticulitis should be direct, but due consideration should be given to the fundamental principles of surgery. The bowel is infected, and there should be resolution of the infection prior to surgical excision. There is increased risk, not only from the standpoint of morbidity but also from the standpoint of mortality when the operation is performed in an infected field. In the development of the surgical treatment of diverticulitis the factor of infection led to the utilization of proximal defunctionalizing colostomy or an exteriorization procedure. However, it has been found that the concomitant use of antibiotics has made it possible to resect the diseased colon initially in selected

patients. Nevertheless, complete reliance should not be placed on the newer drugs.

Resection of the bowel for diverticulitis is not carried out under the same circumstances as that for carcinoma. The field is always potentially infected, and anastomosis of the bowel is subject to the dangers of leakage. It has been my experience that there is a high incidence of anastomotic leakage in primary resection of the left portion of the colon for carcinoma. Proximal colostomy has made the operation a safer procedure, and has prevented the development of any generalized peritonitis. This is especially applicable to anastomoses below the peritoneal reflexion, where there is no strong seromuscular layer to secure the suture line. Antibiotics also have shortened the time that must elapse between colostomy and resection of the colon; the former delay of 6 to 12 months has been reduced to 6 to 12 weeks. A long period of semi-invalidism after colostomy is not necessary today.

It is generally accepted that diverticulitis has no direct relationship to the development of cancer of the colon. In a few patients the roentgenographic picture of diverticulitis will be difficult to differentiate from that of cancer, and in these patients exploration should be carried out without delay.

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THE APPLICATION OF NECK GLAND RESECTIONS*

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The majority of neoplastic lesions of the mucous membranes of the lip, tongue, mouth, tonsillar areas, and larynx have ulcerated, infected surfaces and a variable number will be accompanied by enlarged regional lymph nodes. These nodes may, or may not be tender, and if the central portion is not suppurating, they can be firm or hard. Fixation to surrounding structures may, or may not be present. Progressive enlargement of a regional node after eradication of the primary neoplasm is strongly presumptive evidence that viable, growing neoplasm is present within the node; yet in such instances one ofttimes finds simple, progressive, suppurative inflammation without evidence of tumor cells. Perhaps just as striking are the instances in which nests of tumor cells are sequestered within nodes, scarcely discernible upon palpation, removed as a routine measure in the treatment of the neoplasm at hand.

These observations lend a degree of uncertainty as to the precise instance in which one must undertake definitive treatment of the regional nodes in each patient with an ulcerative lesion about the head and neck. Moreover, the efficacy of surgical treatment and the mortality rate associated with its accomplishment, in the eradication of malignant deposits within regional lymph nodes, while usually considered highly effective, often is far from ideal.

The general technics for surgical nodal resection are for the most part similar in the large majority of lesions about the head and neck and were the ones utilized during the 20 years from 1934 through 1954 when 522 patients were operated upon at the University of Michigan Hospital for the treatment of known or possible metastatic and inflammatory lesions within lymph nodes of the neck. The primary lesions for which these operations were done and the number of patients with each lesion are shown in table I.

This group of patients has no common denominator other than that some form of neck gland resection was done because of a lesion in the above area. Often the dissection was very limited because of old age, debility, or advanced, unrelated disease. In 12 patients it is to be noted that a primary lesion was never demonstrated by persistent examination or by intense historic review. In order to evaluate totally the operations done upon neck nodes the 4 patients with non-neoplastic diseases were included in this survey.

In the treatment of these 522 patients a suprahyoid neck dissection was done 284 times. On 22 patients this was a unilateral procedure. There was one death conceivably related to the operative procedure and three additional deaths within the three months period immediately succeeding the operation.

A supraomohyoid dissection was done on 35 patients. This operative procedure was accompanied by no immediate mortality but one death followed discharge from the hospital and again within the three months postoperative period.

* From the University Hospital, Ann Arbor, Michigan.

TABLE I

Lip (upper and lower)	269 patients
Tongue	48
Alveolar ridge (upper and lower)	25
Floor of mouth	17
Buccal mucous membrane	14
Tonsil, tonsillar pillar, palate	9
Larynx and epiglottis	23
Skin of head and neck	26
Melanoblastoma	23
Thyroid	23
Salivary glands (major and minor)	18
Sarcoma-lymphoma	11
Non-neoplastic disease	4
Unknown primary	12

Two hundred and one patients had the standard radical neck gland resection. Three deaths occurred prior to discharge from the hospital, a surgical mortality rate of 1.5 per cent. Seven additional deaths occurred within three months of operation giving an over-all, conservative death rate of 5 per cent.

Two additional patients must be added. One of these had a resection of posterior triangle nodes (for melanoblastoma) and another a dissection of the parotid area only (for carcinoma of skin of face).

Operations which combined neck gland resection with resection of tongue, mandible, parotid salivary gland, thyroid gland and larynx were done on 56 patients. These operations are shown in table II.

None of these patients died in the immediate postoperative period. However, 2 died within two months of operation of recurrence and rapid progression of their neoplasm and 1 died at three months of hemorrhage and cerebral infarction following ligation of the carotid artery. These three deaths give a gross mortality rate of 5.3 per cent. Not included in this group are patients who had large excisions of neoplasms of the skin or lips when this method of eradication of the primary neoplasm accompanied neck gland resection. These latter operations added little to the operative time and did not seem likely to increase the hazard of the operation in the neck.

TABLE II

Radical neck gland resection and hemimandibulectomy	16 patients
Radical neck gland resection and parotidectomy	9
Radical neck gland resection and thyroidectomy	15
Radical neck gland resection, parotidectomy, hemimandibulectomy	2
Radical neck gland resection, total laryngectomy	7
Radical neck gland resection, tongue, hemimandibulectomy	2
Supraomohyoid neck gland resection, parotidectomy	2
Suprahyoid neck gland resection, hemimandibulectomy	1
Suprahyoid neck gland resection, hemiglossectomy	2
Total	56

TABLE III

Bilateral neck node resections

Primary Lesion	Node Status	Histologic Status Nodes	Survival after 1st Operation	Survival after 2nd Operation	Present Status	
Lip (2 pts.)	Palpable	Positve	6 yrs.		Alive and well	
	Palpable	Positive	2 yrs.	14 mo.	Dead of Ca.	
Tongue (3 pts.)	Palpable	Positive	14 mos.	9 mo.	Dead of Ca.	
	Palpable	Positive	4.5 yrs.	1 yr.	Dead of Ca.	
	Palpable	Positive	3 mo.	—	Dead of Ca.	
Alveolar Ridge (1 pt.)	Absent 1st side Palpable 2nd side	Negative 1st side Positive 2nd side	1 yr.	5 mo.	Dead of Ca.	
Larynx (3 pts.)	Palpable	Positive	10 mo.	8 mo.	Dead of Ca.	
	Palpable	Positive	5 mo.	2 mo.	Dead of Ca.	Laryngectomy with 1st operation.
	Palpable	Positive	8 mo.	6 mo.	Dead of Ca.	
Thyroid (2 pts.)	Palpable	Positive	1.5 yrs.	1 yr.	Alive and well	Thyroidectomy with 1st operation.
	Palpable	Positive	26 mos.	2 yrs.	Alive with Ca.	Thyroidectomy with 1st operation.
Melano-blastoma (1 pt.)	Palpable	Positive	6 mo.	5 mo.	Alive pul-monary metas-tases	
Palate (1 pt.)	Palpable	Positive	2 yrs.	1.5 yrs.	Dead with Ca.	

Thirteen patients had bilateral radical neck gland resections. These were done on patients listed in table III.

CARCINOMA OF LIP

Since this discussion is not concerned with the curability of the primary lesion no attempt is made to separate the lesions of upper lip from those of the lower.

At the University of Michigan Hospital it was the policy for many years to remove routinely the nodes within the suprohyoid and submental triangles after treatment of the primary lip lesion had been completed. Only on those patients with advanced or massive primary lesions, when curability of the primary lesion was in doubt, was neck dissection delayed. In a few instances, 7 in all, the dis-

section was of one triangle only. This latter procedure is admittedly an inadequate one, but age and debility often combined to make this limitation seem urgent. In particular instances extension of the area of dissection was important.

There are 269 patients in this group. Two hundred and thirty-six of these patients had suprahyoid triangle dissection (7 of these were unilateral). There were two deaths, a mortality rate of 0.8 per cent. Omohyoid dissections were done 16 times and radical (complete) neck dissections were done on 17 patients. One patient upon whom the radical dissection was done died one month after operation and is considered an operative mortality (5.8 per cent). All of these patients have been followed to date, but only 226 (84 per cent) have been followed five years or longer. One hundred and twenty-one are alive and well, 102 have died but without evidence of neoplasm in lip or neck, and 45 (16 per cent) have died with their neoplasms. Seventy-three per cent (33 patients) of those dead with carcinoma had neoplasm within the neck at the time of death while 12 patients had recurrent or residual neoplasm in the lip without evidence of tumor deposits in the neck.

Since the policy of prophylactic or routine neck dissections in patients with lip neoplasms has been followed relatively closely it is of interest to note the results of such a course. Insofar as could be ascertained no significant nodal enlargement could be noted in the necks of 147 patients. However, 7 (4.8 per cent) of these had histologic evidence of neoplasm and 3 of these (2 per cent of the total patients in this group) died with carcinoma within the neck. By contrast 122 patients had clinically evident nodes and upon histologic examination 61 (50 per cent) had neoplasm present, and 27 of these, or 44 per cent of these patients with positive nodes, died with tumor in the neck. Thus a total of 68 patients had histologic evidence of neoplasm metastatic within neck nodes and 30 (44 per cent) had residual metastatic neoplasm in the neck at their deaths. It would appear, then, that even though the majority of the operations on the necks of these individuals might be considered inadequate, some protection and the possibility of prolonged survival has been afforded 56 per cent of those with metastases within the neck.

It is of further interest to observe the effectiveness of the types of operation used upon the patients with histologically positive nodes. Forty-three patients were treated by suprahyoid dissection. Nineteen of these (44 per cent) died with carcinoma in the neck. Five of these were unilateral dissections and thus admittedly of limited effectiveness. With these 5 patients deleted 14, or 32 per cent of the patients, died with carcinoma in the neck. Of the 10 patients who had omohyoid neck dissection 6 (60 per cent) died with carcinoma in the neck while 5 (33 per cent) of the 15 patients who had radical neck dissections for positive nodes died of carcinoma. These observations on a small group of individuals are not statistically of significance yet they do suggest that more extensive neck gland resection may not be the sole factor in effecting a profoundly improved survival figure.

To complete the above picture 2 additional patients treated by suprahyoid triangle dissection must be noted. One patient had additional tumor metastatic

within nodes beyond the area of the suprahyoid dissection. This patient was treated by irradiation of the neck, survived three years without recurrence and died an accidental death. Another patient died after three years without neck metastases but with symptoms suggestive of central nervous system metastases.

Three patients are known to have had carcinoma metastatic within the neck at the time of death but positive nodes were not present in the material submitted at the time of their suprahyoid neck gland resection.

From the above observations on patients with lip carcinoma one might enunciate the following treatment program in the care of their regional neck nodes:

1. The incidence of carcinoma within nodes, not evident upon clinical examination, is low (4.8 per cent in this series) and routine neck gland resection does not seem a worthwhile undertaking.

2. The incidence of carcinoma within nodes, clinically evident, is high (50 per cent in this series) and in this group some form of definitive treatment must be instituted.

It does seem important at this point, although commonplace and hackneyed, to observe that any form of neck gland resection, regardless of its extent, is adequate as long as its limits are beyond the tumor-bearing nodes. It is perhaps for this reason that the supraomohyoid resection has been popularized. When the nodes beyond the hyoid triangles are found to be negative then the dissection has been satisfactory. Too often it is not recognized that when the nodes of the carotid sheath contain neoplasm this area of resection is not sufficient and a more complete neck dissection is required.

3. In most instances of lip carcinoma bilateral gland resections are advisable.

4. Supraomohyoid dissection is the most desirable procedure to be done. If the primary lesion does not approach the midline the opposite side dissection may be of lesser extent, e.g. a suprahyoid triangle dissection.

5. Whenever the carotid sheath nodes contain metastatic neoplasm, either on rapid or permanent section examinations, a complete or radical neck dissection is indicated.

TONGUE

There were 48 patients in this series. Within the last decade an increasing tendency to resect the regional nodes in all patients with carcinoma of the tongue has been apparent. Seventeen patients of this series, 35 per cent, did not have clinically suggestive or apparent nodes within the neck at the time of neck gland resection. In 6 patients one or more of the resected nodes contained metastatic carcinoma; thus, 1 out of 3 of those patients, not suspected from examination of the neck of harboring metastatic carcinoma within cervical nodes did so.

Twenty-one patients with palpable cervical nodes were subjected to neck node resection and 26 (84 per cent) had histologically positive nodes.

In this group of 48 patients two-thirds had metastatic carcinoma within neck lymph nodes. However, it must be pointed out that no observation is available upon the total number of patients, seen in this same 20 year period, who had no operation upon the neck. It is to be expected that the patients with large lesions of long duration will be the individuals most likely to have metastatic

carcinoma within neck nodes and the patients most surely to be offered operations upon the nodes. In this respect the high incidence of positive nodes is misleading.

In this group of patients the operations done are weighted in favor of the more extensive resections. Thus, 37 of these patients had complete or radical gland dissections. There was one postoperative death. Seventeen of these patients (45 per cent) are alive and well without evidence of tumor but only 4 of these have survived 5 years or longer. Moreover, only 6 had histologically positive nodes and 3 of these had one positive node only; 1 patient had two nodes, another three and the last five positive nodes in the resected specimen.

Twenty of the 37 patients upon whom complete dissections were done are now dead. Five have died of causes other than carcinoma of the tongue or metastatic carcinoma therefrom.

Fifteen of the patients of this group have died of carcinoma. One of these was the operative death. Ten (27 per cent) have died with carcinoma in the neck and 4 from recurrent tongue carcinoma. Seven of the 10 patients dying with carcinoma in the neck had obvious neoplasm within venous channels or extensive tumor in adipose tissue and muscle. This is in sharp contrast to the minimal deposits of metastatic tumor in the surviving patient group.

Four patients had bilaterally extensive neck dissections (table IV). Only 2 patients had procedures in which radical neck dissection was combined with resections of tongue, of floor of mouth or mandible (table V).

TABLE IV

Bilateral extensive node resections, tongue

Patient	Operation	Status of Nodes	Survival after 1st Operation	Survival after 2nd Operation	Present Status
1	Radical dissection	Positive			
	Radical dissection	Positive	14 mo.	9 mo.	Died of Ca.
2	Radical dissection	Positive	54 mo.	12 mo.	Died of Ca.
	Radical dissection	Positive			
3	Bilateral radical dissection; hemimandibulectomy; glossectomy	Positive	3 mo. (one operation)		Died of Ca.
4	Supraomohyoid	—		7 mo.	Died of Ca.
	Radical dissection	Positive			

TABLE V

Combined resections, tongue

Patient	Operative Procedure	Status of Nodes	Follow-up Period	Present Status	
1	Bilateral radical dissection mandible; tongue.	Positive	3 mo.	Dead of Ca.	(see preceding table)
2	Unilateral radical dissection mandible; tongue	—	6 mo.	Alive and well	

Three patients were treated by supraomohyoid dissection. Only 1 of these patients had clinically evident nodes and none of them had metastatic carcinoma within nodes. Since operation 2 have died with carcinoma within neck tissues and 1 survived three years and died of carcinoma of the stomach.

Eight patients were treated by suprahyoid triangle dissection. Five of these

TABLE VI

Intra-oral carcinoma

Operation Type	Node Status	Early Deaths	Later Deaths (3 mo.)	Alive and Well	Death, No Carcinoma	Death, Neck Carcinoma	Death, Primary Carcinoma	Alive, Cancer Present	Summary
Alveolar ridge carcinoma—25 patients									
Suprahyoid, 6 pts.	5 (pos.)	0	0	1 (neg. nodes)	—	5	0	0	11 patients alive and free of tumor at 6, 8, 8 mos., 1.75, 3, 3, 3, 3.5, 6, 6, 8 years.
Supraomohyoid, 3 pts.	3 (pos.)	0	0	1	—	1	1	—	—
Radical 8 8 pts.	6 (pos.)	1	1	4 (2 neg. nodes)	—	3	—	—	
Combined operation, 8 pts.	5 (pos.)	0	0	5 (3 neg. nodes)	1[x]	2*	—	—	Note: [x] — melanoblastoma. * — bilateral resection, 1 pt.
Buccal mucosa carcinoma—14 patients									
Suprahyoid, 6 pts.	5 (pos.)	0	0	1	2[z]	3	—	—	4 patients alive and free of tumor at 2, 7, 7, 13 years.
Supraomohyoid, 1 pt.	1 (neg.)	0	0	1	—	—	—	—	Note: [z] — dead at 10 yrs. with ca. rectum; coronary occlusion at 3 yrs. [y]— Ca. lung.
Radical, 5 pts.	4 (pos.)	0	0	2 (1 neg. nodes)	1[y]	1	1	0	
Combined, 2 pts.	2 (pos.)	0	0	0	0	1	—	1, extensive	

TABLE VI—*Continued*

Operation Type	Node Status	Early Deaths	Later Deaths (3 mo.)	Alive and Well	Death, No Carcinoma	Death, Neck Carcinoma	Death, Primary Carcinoma	Alive, Cancer Present	Summary
Floor-of-mouth carcinoma—17 patients									
Suprahyoid, 5 pts.	all neg.	1[a]	0	1	0	0	3	0	4 patients alive and free of tumor at 1 mo., 1, 5, 5 years.
Supraomohyoid, 3 pts.	all neg.	0	0	0	0	2	1	0	Note: [a] — postoperative death with F. A. tuberculosis.
Radical, 6 pts.	5 (pos.)	0	0	2 (1 neg.)	0	4	0	0	
Combined, 3 pts.	3 (pos.)	0	0	1	0	2	0	0	
Carcinoma, tonsil—3 patients									
Radical, 3 pts.	3 (pos.)	0	0	0	0	2	0	1	
Carcinoma, Palate—3 patients									
Suprahyoid, 1 pt.	1 (pos.)	0	0	0	0	1	0	0	unilateral dissection —79 yrs.
Radical, 2 pts.	2 (pos.)	0	0	1	0	1*	0	0	Note: *— bilateral resection alive, well 1 yr.
Carcinoma, tonsillar pillars—2 patients									
Suprahyoid, 1 pt.	1 (neg.)	0	0	0	0	0	1	0	survived 9 yrs.
Radical, 1 pt.	1 (neg.)	0	0	1	0	0	0	0	alive, well 2 yrs.
Carcinoma, hypopharynx—1 patient									
Radical, 1 pt.	?	0	0	1	0	0	0	0	alive, well 5 yrs.

Combined operation indicates complete neck dissection and hemimandibulectomy.

had palpable nodes and 3 had histologically positive nodes None of the patients without palpable nodes had positive nodes on histologic section.

Three of these patients had combined resections; in 2 instances a hemoglossectomy was done and in 1 a hemimandibulectomy in addition to the limited neck

dissection The 2 patients with neck node and tongue resections died of carcinoma at 7 months and 24 months, but in each instance the recurrence was in the tongue.

Only 1 patient in the suprahyoid group has been followed more than five years and this patient died of his carcinoma. Only 2 patients are alive at 6 months and 24 months, but neither had metastatic carcinoma within the nodes resected.

This group of patients is a small one and to deduct any arbitrary information from it is not possible. Yet, from the information present several suggestions are made: 1. Two of every 3 patients in the total group reported with carcinoma of the tongue had metastatic carcinoma within regional neck nodes. 2. The incidence of metastatic carcinoma in neck nodes is very high in patients with clinically apparent nodes. One of each 3 patients without palpable nodes also had carcinoma within these nodes. 3. Complete or radical neck gland resection is the more satisfactory operation in patients with carcinoma of the tongue. Bilateral complete neck gland resection, in one or two stages, has not been a staisfactory operation in our hands.

INTRAORAL CARCINOMA

Sixty-five patients, tabulated in table VI had intraoral carcinoma other than of the tongue. Twenty-two of these patients are alive and free of their original neoplasm. However, only 12 of these 22 patients had known metastatic tumor deposits within lymph nodes (table VII).

These groups of patients are again small and the impressions gained from each are of limited value. Of the three larger groups of patients the over-all survival of patients with floor-of-mouth carcinoma seems least good. When the type of operation done in the presence of nodal metastases is compared (table VIII) it is apparent that the suprahyoid resection is the least adequate opera-

TABLE VII

Intraoral carcinomas—survival groups

	Patients	Positive Nodes	Total Survivors	Survivors with Positive Nodes	
Alveolar ridge	25	19	11	5*	* One additional pt died of another lesion.
Buccal mucosa	14	11	4*	2	* Three additional pts. have died of other lesions. (Ca. lung; Ca. rectum; coronary occlusion)
Floor of mouth	17	8	4	3	
Tonsil	3	3	0	0	
Palate	3	3	1	1	
Tonsillar pillars	2	1	1	1	
Hypopharynx	1	?	1	?	
Totals	65	45	22 (33%)	12 (26%)	

TABLE VIII

Intraoral carcinoma

Operation	All Patients		Positive Nodes	
	Total number	Alive—well	Total number	Alive—Well
Suprahyoid dissection	19	3	11	2
Supra-omohyoid dissection	7	2	3	1
Radical resection	26	11	21	6
Combined resection	13	6	10	3

tion. This is the anticipated conclusion. Perhaps the most gratifying feature of this comparison is the observation that the survival rate of patients, with composite operations, in which the primary lesion in buccal mucous membrane, alveolus or floor-of-mouth was removed along with the hemimandible and regional lymph nodes, compares favorably with the survival rate of the less extensive operation of radical neck node resection. This is, of course, expected when it is recalled that in about 50 per cent of normal individuals lymphatic from the floor of the mouth (and tongue) pass through the periosteum of the mandible.

CARCINOMA OF LARYNX AND EPIGLOTTIS

There were 23 patients in this group. All had radical gland resections. The majority were treated by members of the Department of Otolaryngology at the University of Michigan. Treatment of these patients falls readily into three categories.

A) Primary lesion irradiated—neck dissected when nodes appeared.
7 patients—3 patients alive and well at 0.5, 4.5 and 5.5 years.
2 patients died but not with carcinoma at 3.5, 5 years.
2 patients died with carcinoma at 10 mo.,* 1 year.

B) Total laryngectomy followed at later date by neck gland resection.
9 patients—1 patient alive and well after 3 years.
1 patient alive with carcinoma after 9 months.
7 patients died with carcinoma at 4, 5, 7, 7*, 8*, 9 mo. and 2 years.

C) Combined laryngectomy and radical neck gland resection.
7 patients—3 patients alive and well after 1, 2, 3 years.
4 patients died with carcinoma after 0.5, 1.5, 1.5 and 2 years.

It seems apparent that the best survival figures are from those patients whose primary lesion was treated by irradiation and the neck nodes resected at a later date. All of the patients in this particular category had histologically positive nodes.

* These patients had bilateral, staged radical neck gland resections. The underlined survival periods indicate that metastatic carcinoma was present in the gland-bearing tissues removed.

TABLE IX

Carcinoma of thyroid—combined operations

	Alive, No Known Tumor	Alive, Known Tumor	Dead with Tumor	Dead, No Tumor	
Combined radical dissection and thyroidectomy	9			1[a]	[a] —Died during herniorrhaphy
Thyroidectomy followed by radical dissection	6	1	2		
Thyroidectomy, radical dissection; radical dissection	1[x]	1[y]			[x]—alive 2 yrs. after 1st operation, 1 yr. after 2nd. [y]—2 yrs. after operation.
Thyroidectomy; infrahyoid dissection	1			1*	*—age 79 yrs.

THYROID CARCINOMA

Neck gland resections are recorded on 23 patients with carcinoma of the thyroid. In this group of patients only 2 are known to have died of their carcinoma, 2 are alive with residual neoplasm still present within the neck tissues and 2 patients have died of other diseases without obvious residual thyroid tumor. One patient only in this group had no tumor within the neck nodes. All of the remainder had histologic evidences of metastatic tumor.

Seventeen patients now survive without evidence of their carcinoma (table IX). This appears to be an excellent survival rate but may be an overly optimistic observation in view of the insidious and slow growth of this tumor in many patients. Moreover, with the increasing use of I^{131} as a diagnostic tool as well as a therapeutic agent it can be anticipated that earlier detection of these tumors may be possible and that in some instances residual tumor deposits may be eradicated when they make their appearance after nodal excision has been done.

These neck resection figure would be considerably more significant if the interval between operation and this writing was greater. Only eight of these patients were operated upon more than three years ago and only 3 have survived longer than five years. Nevertheless, this is, in general, an encouraging picture and hope for improvement and for longer term results is good.

The selection of patients for nodal resection has been well crystallized:

1. At the time of thyroidectomy, if carcinoma of the thyroid is detected, nodes are removed from along each jugular chain at a site near the entrance of the lateral thyroid veins into the jugular veins.

a) If positive nodes are present, upon frozen section examination, a dissection of the nodes may be done at that time.

b) If bilaterally positive nodes are present resection of those of one, the most involved side, is done and I^{131} uptake studies on the contralateral side are made in the postoperative period. If uptake is poor a resection of the nodes on this side is done after an arbitrary six weeks interval. If uptake is excellent a treatment dose of the isotope is given and neck dissection done only if this is ineffectual.

TABLE X

Salivary gland neoplasms

Squamous cell carcinoma	4 patients
Pseudoadenomatous basal cell carcinoma	4
Adenocarcinoma	2
Medullary (undifferentiated) carcinoma	3
Mucoepidermoid carcinoma	1
Serous cell adenocarcinoma	1

It would appear from this small group of patients that waiting for the appearance of nodal enlargement, before neck gland resection is done, is a somewhat less desirable course.

SALIVARY GLAND TUMORS

There were 18 patients in this group. Ten of these had a primary lesion of the parotid gland, 6 a lesion of the submaxillary or sublingual gland and 2 had carcinomas arising in the lesser or minor salivary glands. Three patients were ultimately judged to have had benign lesions. Eight of these patients are alive and without tumor but only 3 had histologically positive nodes and only 2 have survived five years or longer. Fifteen patients had lesions which were malignant and thought capable of metastasizing. The primary tumors are listed in table X.

The mucoepidermoid carcinoma had no nodal metastases and since this tumor is separated best from its benign counterpart by the presence of metastases this may well be considered a benign lesion. The serous cell adenocarcinoma does not, in our experience, metastasize by way of lymphatic channels, and did not in the one patient show evidence of nodal metastatic tumor. Nine of the remaining 13 patients had regional node metastases and of these 3 are living and well while 1 additional patient died seven years postoperatively of another lesion without evidence of his original neoplasm.

Ten of these patients were treated by radical neck gland resection. In 6 of these removal of the neck nodes was continuous with removal of the parotid salivary gland and in 2 with removal of the parotid gland and a portion of the mandible. Five of these patients are alive and well. Two of the living patients had regional node metastases.

Four patients had a supraomohyoid gland dissection and in 2 this was continuous with parotidectomy. Three of these patients are alive and well 4, 5 and 12 years later. Only 1 had regional nodal metastases.

Four patients had dissection of their suprahyoid triangles. None is alive at this moment. Two died, each four years after operation, without evidence of their original neoplasm.

The indications for neck gland resections in this particular group of patients are difficult to define. Much of the disorder lies in the varied and confusing terminology used in describing the salivary gland tumors. Moreover, the peculiarities of spread beyond the primary site are not well understood. For example, the serous cell carcinoma is disseminated almost exclusively by way of blood channels. By contrast the pseudoadenomatous basal cell carcinoma is a slowly

growing, almost inexorable, lesion which frequently spreads by both vascular and lymphatic routes. The mucoepidermoid tumors are difficult to classify as malignant until metastases are found within regional nodes. Two of the three patients who had undifferentiated tumors described died within less than one year of their operations with widespread local and distant metastatic foci and might have been treated better by irradiation rather than by surgical removal of the neck nodes.

Neck gland resections done ideally in continuity with removal of the salivary gland, appear most logical in patients with well differentiated squamous cell carcinoma and in that small group of patients whose adenocarcinomas are composed of acidophilic or oxyphilic cells. This latter tumor appears to be disseminated most often by way of lymphatic routes. The more limited dissection of the suprahyoid area is not ideal; certainly for the highly malignant squamous cell carcinomas radical surgical measures are demanded to effect eradication.

MALIGNANT SKIN LESIONS

Two categories of lesions appearing within the skin are considered under this heading. These are the squamous cell carcinomas and the malignant melanomas or melanoblastomas (table XI).

In considering these lesions as they occur about the head and neck the surgeon is inclined to give a considerably better prognosis to the squamous cell neoplasms. It is gratifying then to note that the outlook for patients with melanoblastomas is far from a hopeless one; for patients in this tiny series an almost identical outcome has been afforded those with regional node metastases.

TABLE XI

Postoperative status

	Positive Nodes				Negative Nodes			
	Alive and well	Alive with Ca.	Dead with Ca.	Dead without Ca.	Alive and well	Alive with Ca.	Dead with Ca.	Dead without Ca.
Melanoblastoma—23 patients								
Radical gland resection	4	1	5		4	1	4	
Supra-omohyoid dissection			2					
Suprahyoid dissection			1					
Post. triangle resection			1					
Squamous cell carcinoma skin—26 patients								
Radical gland resection	2		3	1*	1		1×	3× 1*
Supra-omohyoid dissection			1		1			
Suprahyoid dissection			5		3			3
Parotid node resection	1							

* 2 patients died in immediate postoperative period—operative deaths.

× Death with recurrence and extension of primary lesion.

From the 23 patients with melanoblastomas 8 are alive and well from one to seven years after nodal resection. Four of these had regional lymph node metastases. A like number have survived 1 to 12 years after operation from among the 26 patients with squamous cell carcinoma.

Three of the patients with melanoblastomas had combined resection of their parotid glands (and parotid lymph nodes) along with radical neck gland dissection. One of these had positive neck nodes and all 3 are alive and well 2, 7 and 7 years. One patient had bilateral complete neck dissections and now, six months later, has pulmonary metastases.

One of the patients with squamous cell carcinoma of the skin of the ear had a combined resection of ear, parotid salivary gland and radical resection of neck nodes. He died 20 months later with local and regional recurrences.

In general the patients reported here support the usually accepted conclusion that only a radical removal of regional lymph nodes should be entertained for those patients with metastases from melanoblastomas and a similar conclusion seems just in those patients who have nodal metastases from squamous cell lesions. Resection in continuity is desirable wherever possible.

SARCOMAS

The heading of "*Sarcoma*" is one of convenience since under it are grouped 2 patients with lymphosarcoma, 1 patient with rhabdomyosarcoma, 3 patients with spindle cell sarcoma, 3 patients with hemangio-endothelial sarcoma, and 2 patients with lymphoblastoma. All of these patients had radical neck gland resections. There are 11 patients so listed of whom 9 died of their neoplasms, another died without evidence of recurrent tumor and 1 is alive with known residual endothelial sarcoma. Only 3 patients lived longer than 1 year after operation; the 2 patients with lymphoblastoma lived 1.5 and 5 years and the 1 patient with a rhabdomyosarcoma lived 2.5 years. All 3 now are dead.

In addition to complete resection of neck glands 4 patients had resections of the thyroid gland (2 patients), the mandible and the parotid gland. There were no immediate deaths but 2 patients died within one month of operation.

This group of patients is a record of total failure. In general, regional neck gland resections are not particularly suited for lesions of this type. The operation was commonly done as a means of wide resection of the primary tumor and this appears to be the major indication for such an operation.

UNDISCOVERED PRIMARY TUMORS

The application of neck gland resection in these 12 patients is contrary to the usual concept that such operations are reserved for those in whom "the primary lesion is controlled or controllable" (table XII).

Commonly these patients were seen because of a lump in the neck. Upon biopsy eight lesions were diagnosed squamous cell carcinoma, two as undifferentiated carcinoma and one a papillary carcinoma. This last patient may harbor a primary lesion within the thyroid gland but in the five years following operation this is not yet apparent. One other patient had a cystic lesion. Upon histologic section it was suggested that this might be an adenocarcinoma arising in a

TABLE XII

Unknown primary tumors—postoperative status—12 patients

	Alive and Well	Alive, with Tumor	Dead with Carcinoma	
Radical node resection	2	3	3	
Suprahyoid node resection	1		2*	*—unilateral triangle dissections.
Supra-omohyoid node resection	1x			x—primary may have been carcinoma in branchial cleft cyst.

branchial cyst. No additional tumor was present and the patient has survived 14 years.

Justification for these operations upon patients in whom a prolonged search has failed to reveal the primary tumor lies in the survival of 4 of them for 3, 4.5, 8 and 14 years. Another patient, who ultimately succumbed from his carcinoma, did so after 11 years; his nodal resection was a unilateral one of the suprahyoid triangle and his long survival can be attributed to repeated, intensive irradiation.

In the absence of a recognized primary source for these metastases there is much justification for considering them incurable lesions. Yet the occasional patient who survives a long period supports the suggestion that when such circumstances exist, and an intense survey fails to reveal a parent lesion, the surgeon is justified in eradicating the metastatic foci by whichever operative procedure seems most certain of effecting a cure, and undertaken as though the source were known and well controlled. It must be recognized that there will be few instances indeed in which this will be a rewarding operation.

NON-NEOPLASTIC LESIONS

Four patients are recorded in this final group. Two of these patients had cervical tuberculosis. Upon one a complete neck dissection was done and upon the other a bilateral removal of the nodes in the suprahyoid and submental triangles. In one of these patients the antibiotic drugs had failed to eradicate the disease while the other patient was operated upon prior to the advent of these drugs. These patients have survived 3 and 15 years.

Upon one patient a suprahyoid dissection was done 14 years ago for a submaxillary gland abscess. This patient is well.

The final patient had a radical neck gland resection two years ago because of a diagnosis of carcinoma of the thyroid gland. Subsequent review of the original histologic sections has failed to support this diagnosis.

SUMMARY

The cure rates reported in this survey undoubtedly could be improved remarkably if the neck node dissections had been done earlier in the course of

metastatic malignant disease rather than waiting until more extensive involvement of neck structures has taken place. In some instances one is impressed by the feebleness of the treatment used; this is strikingly apparent in those patients with limited neck node resections who have showed a prompt and often widespread growth of tumor within the neck within a short period after operation.

Much of the material in this review supports the observation that a variable number of patients, often very few, will demonstrate metastatic foci within nodes unsuspected of harboring them. Ideal treatment can be defined as neck gland resection before metastases are apparent to the clinician and well before the tumor has broken through the nodal capsule. This dictum carries the unfortunate burden of the needless surgical removal of nodes from the necks of a large number of patients with the attendant morbidity and mortality which accompanies such operations. A crucial factor in the decision to do neck gland removal along this line lies in the recognition that this is the period in which the cure rate for neck dissection is highest. It is suggested that such a procedure be considered for patients with carcinomas of the tongue, alveolar ridge, buccal mucosa, floor of mouth, thyroid, certain carcinomas arising in salivary glands, and patients with malignant melanomas. Some selection must be admitted for all of these patients, and in many instances resection of neck nodes not combined with removal of mandible, cheek or floor of mouth must be considered as an inadequate and ill considered measure. Carcinomas of the lips, of the skin of the face, head and neck, and of the intraoral locations may be considered somewhat less aggressive lesions from which lymph node involvement occurs late in the course of the disease and frequent, closely spaced observations will permit the recognition and prompt removal of enlarging neck nodes. Whenever and wherever such a policy cannot be followed invariably expeditious resection of regional cervical nodes must be urged upon these patients.

The observation of a higher cure rate for neck gland removal in patients with carcinoma of the larynx in which the primary was treated initially by irradiation is an interesting one and cannot be accepted without qualifications until a larger number of patients can be accumulated.

Sarcomas and lymphoblastomas in the neck, when of small size or limited to a single node or small group of nodes, are readily accessible to thorough surgical excision with the expectation of a staisfactory cure rate. Such a state was not attained in the series of patients reported here and the results correctly reflect the unsatisfactory selection of patients for operation.

It appears likely that there will be an ever diminishing number of patients subjected to extensive neck gland removal for inflammatory disease. The surgical removal of tuberculous nodes has been reduced already to a remarkably small number of patients. In properly selected instances limited resection of tuberculous nodes will result in promary healing.

The immediate postoperative mortality rate reported here is low and can be reduced further only by an increasingly critical selection of patients and type of operation. One of 284 patients who had suprahyoid lymph node resection died in the immediate postresection period, a mortality rate of 0.3 per cent. None of

the 35 patients who had supraomohyoid gland resections died immediately following operation. Of 201 patients upon whom radical neck gland resections were done 3 died prior to hospital discharge giving a mortality figure of 1.5 per cent.

There were no immediate deaths after 54 composite resections which included mandible, tongue, parotid gland or thyroid gland along with the regional nodes. Similarly, no immediate deaths occurred after bilateral complete removal of neck nodes. All but one of these was a staged procedure.

When an arbitrary period after operation, for example three months, is accepted as within the immediate postoperative period then additional deaths will and have accrued in all categories of operation.

It seems likely and desirable that the supraomohyoid dissection will be used with increased frequency and effectiveness in the future and most likely this will be done at the expense of dissections of the suprahyoid triangles.

A more careful and critical selection of patients for bilateral complete node resections must be undertaken. The survival period after operation in the group of patients reported was distressingly short and suggests that in many of these the chance of effective cure had long passed at the time the operation was begun.

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IRRADIATION FIBROMATOSIS AND FIBROSARCOMA

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Many reports of malignant changes in tissues subjected to irradiation have constantly been cited since the early days of the use of radiation for diagnostic or therapeutic purposes. Although much attention has been given the change commonly seen in epithelial tissues, less notice has been given to changes in connective tissue, although fibrosarcoma was first reported by Perthes (cited by Jones[2]) following repeated irradiation for lupus vulgaris over 50 years ago. The recent emphasis on the changes in connective tissue has stimulated the interest of many pathologists and clinicians and prompts this report of 3 cases. The conditions described in these 3 patients are not unique but are relatively rare and are interesting because the diagnosis of epithelioma was made preoperatively in all 3 and the histologic findings came as a surprise.

CASE REPORTS

Case 1. E. K., a 77 year old white woman was admitted to the hospital April 23, 1954, with the complaint of a tumor of her lip and chin. In 1933 she had received irradiation therapy for excessive hair on her face. In 1951 some dark brown crusts formed over her chin and six months before admission a nodule developed in the right lower lip and adjacent cheek where it gradually enlarged and became progressively sensitive to touch.

Examination showed a somewhat obese elderly woman of short stature. The skin showed many changes of chronic dermatitis with maceration, redness and encrustation beneath the breasts and a red scaly dermatitis of the abdomen and lumbar regions. There was considerable swelling of the right lower lip and adjacent cheek with a palpable tumor mass approximately 3 by 2 by 2 cm. Multiple radiodermatic changes with sclerosis, atrophy, telangiectases, keratoses, papillomas, and some black and brown encrusted ulcerations were present over the chin, lips, and cheeks with the greatest changes over the chin (fig. 1). The midthoracic spine was kyphotic and there were crepitant rales at both lung bases. Cardiac examination showed systolic murmurs with some irregular premature beats.

Laboratory examination showed normal findings for the complete blood count, urinalysis, serology, nonprotein nitrogen, creatinine, and sugar. There was some left axis deviation on the electrocardiogram. Roentgenologic examination of the chest showed some cardiac enlargement and pulmonary fibrosis.

At operation on April 24, 1954, with a preoperative diagnosis of epithelioma based on radiodermatitis, the entire lower lip on the right was excised through and through down to the submaxillary fossa. A triangular flap, after the method of Abbe and Estlander, was turned 180 degrees to help fill the defect of the lower lip and chin. Not all of the involved skin could be excised medially at this time. The wound healed without incident. On readmission, August 24, all of the skin of both lips, the chin, and submental regions down to the level of the hyoid was excised and replaced with a split graft cut by the dermatome .025 inches in thickness with nearly 100 per cent take of the graft. Subsequent contracture of this graft required the insertion of a full thickness graft 7 by 4 cm. at the vermillion

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border and just beneath it to allow the lip to come up into a more normal position. The pathologist's diagnosis was fibrosarcoma and basal cell carcinoma.

There has been no local recurrence of the fibrosarcoma or the basal cell carcinoma following the wide initial resection. The patient is satisfied with the cosmetic result although it could be improved.

Pathologic Findings. The specimen from the lower lip was wedge shaped, measured 5.5 by 4 by 3 cm., and weighed 20 grams. A shallow ulcer, 2.5 cm. in diameter, was present along the vermillion border of the lip and skin. Beneath this ulcer, the lip was thickened, and had a firm, rubbery consistency. To one side and below the vermillion border was a second ulcer .5 cm. in diameter; the surrounding skin had a whitish-grey color. On section through the larger ulcer, a circumscribed, nonencapsulated, yellowish-white, firm tumor 2.5 cm. in diameter occupied most of the lip (fig. 2). Microscopically, irradiation changes were evidenced by atrophy of the skin and appendages, telangiectasia of the vessels of the mucous membrane, decrease in number and atypism of the nuclei of the stroma, and atrophy

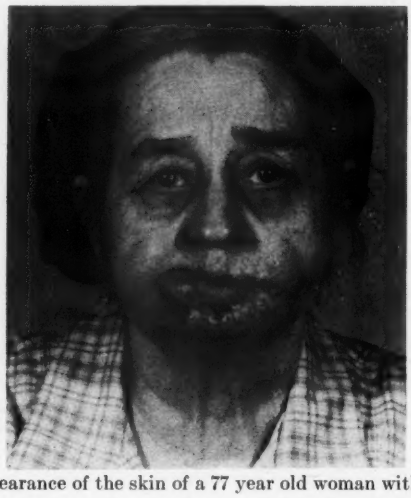

FIG. 1. Case 1. Appearance of the skin of a 77 year old woman with obvious radiodermatitis of long standing.

and fibrosis of striated muscle. The tumor was composed of spindle cells arranged in interlacing bundles. The intersections between bundles formed obtuse angles as well as rather acute angles (fig. 3). In most areas, considerable collagen was present, whereas in other areas the tumor was quite cellular. The nuclei in the cellular areas usually were large, oval, with clumping of chromatin and with somewhat prominent nuclei (fig. 4). Occasional abnormal mitotic figures were found. Some degenerating muscle fibers and multinucleated giant cells were found in the tumor. About the edge of the tumor, muscle was being incorporated by extension of the spindle cells between the muscle bundles and fibers. Foci of lymphocytes were generally seen at the periphery; however, a few were scattered throughout the tumor. Usually there was a gradual transition between the surrounding stroma and tumor cells. The epithelium appeared to have no connection with the tumor. The small ulcer at the edge of the larger lesion was found to be an infiltrating basal cell carcinoma which had many points of communication with the overlying epithelium. Considerable desmosplasia was noted about the nests of carcinoma cells. The basal cell carcinoma and fibrosarcoma were separated by well differentiated fibrous tissue (fig. 5). In the area of sarcoma Laidlaw silver stain revealed individual tumor cells to be surrounded by reticulum

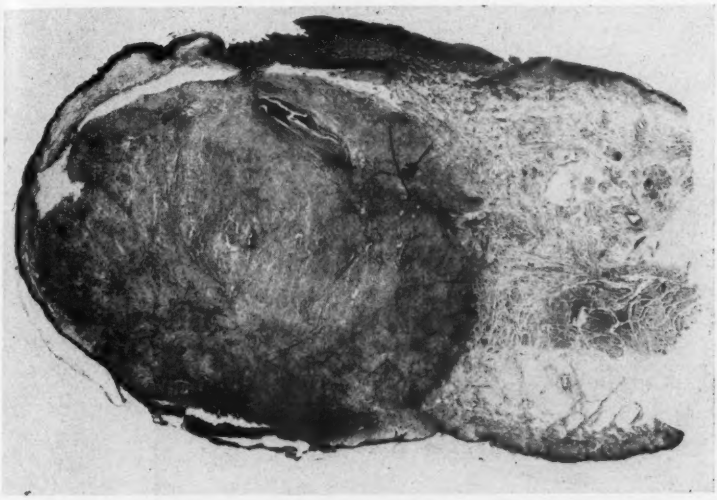

FIG. 2. Case 1. Vertical section through lower lip at the edge of large ulcer and ovoid tumor mass. Hematoxylin and eosin stain. × 3.5.

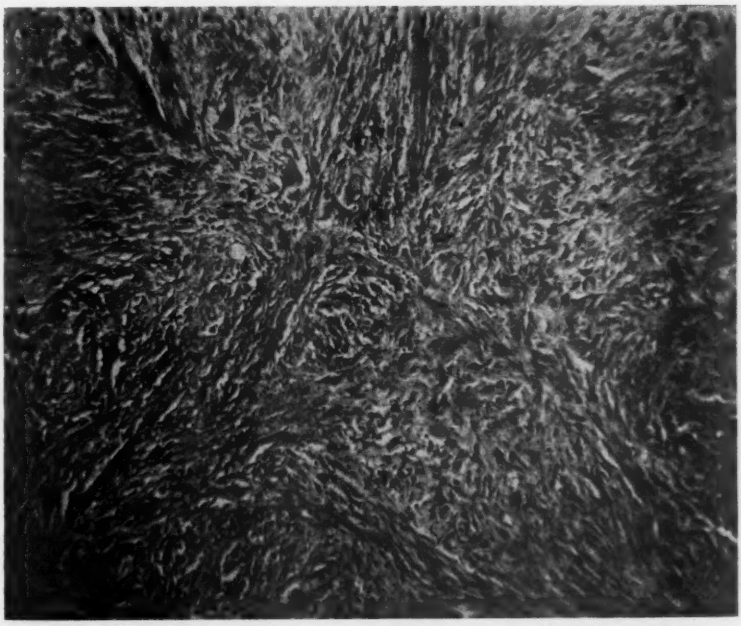

FIG. 3. Case 1. Section from the center of the tumor shows interlacing bundles of spindle cells with varying degrees of maturation. Hematoxylin and eosin stain. × 33.

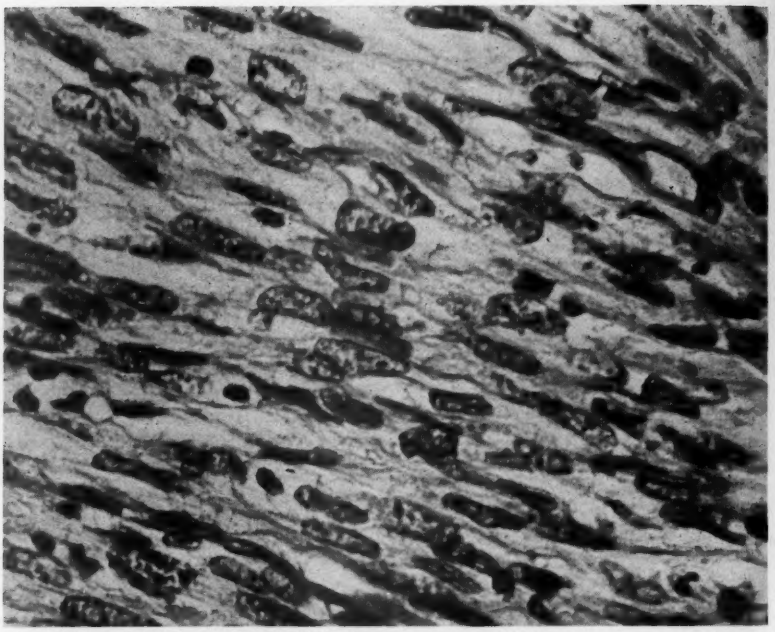

FIG. 4. Case 1. Higher magnification through a more cellular area shows moderated irregularity in size, shape, and staining of the nuclei. Hematoxylin and eosin stain. × 660.

fibers. In contrast, the nests of carcinoma cells were surrounded by a sheath of reticulum as though pre-existing reticulum had been pushed before the expanding groups of tumor cells.

Case 2. F. B., a 93 year old white man was admitted to the hospital April 21, 1954, with a complaint of a *"sore"* on the tip of his nose for the past year. Within the preceding five years he had had several *"skin cancers"* removed by radiotherapy. The type and dosage are not known. Five months before admission a course of roentgen therapy had been given to the nose and, because of an increase in size of the lesion, three more treatments were given two months before admission.

Examination showed an asthenic, elderly, white man of advanced age, showing general degenerative changes but nothing unusual except the lesion on the tip of the nose. A nodular indurated mass 2 cm. in diameter at the end of the nose was covered with scaly and keratotic skin (fig. 6).

Laboratory examination, including complete blood count, urinalysis, nonprotein nitrogen, creatinine, and serology, demonstrated all findings within normal limits. An electrocardiogram showed left axis deviation and incomplete left bundle branch block. Roentgenologic examination of the chest showed pulmonary emphysema and osteoarthritis of the dorsal spine.

The preoperative diagnosis was epithelioma of the nose. Operation was done on April 24, under local procaine anesthesia. The tip of the nose was excised with the electrosurgical unit. Three days later when the original dressing was removed, the patient was dismissed. Living some distance from the Medical Center and being of advanced age, he did not return for follow-up examination, but it was reported that the lesion apparently did not recur. In answer to a follow-up letter, it was stated by his daughter that, following a fall and fracture of an arm, he died Jan. 1, 1955.

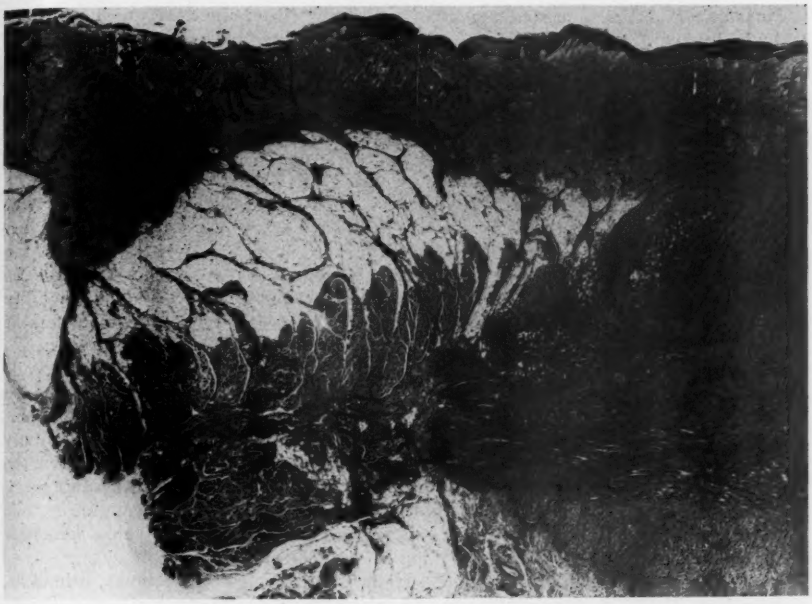

FIG. 5. Case 1. Horizontal section through the lip shows the fibrosarcoma invading striated muscle in the right center of illustration. The ulcerated basal cell carcinoma is in left upper, and nonulcerated carcinoma is in the upper center. Hematoxylin and eosin stain. X 8.

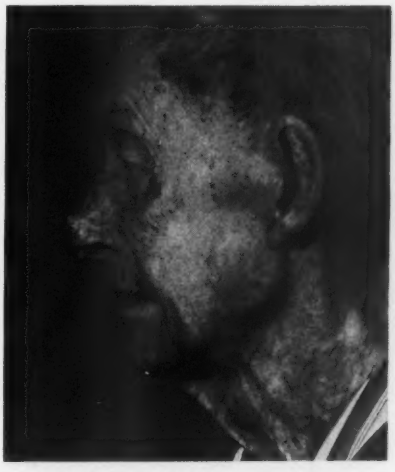

FIG. 6. Case 2. Multiple radiodermatitic changes over the nose of a 95 year old man who had received considerable radiation therapy for carcinoma within the preceding five years.

Pathologic Findings. The specimen consisted of the tip of the nose which measured 3.5 by 1.5 by 4 cm. A triangular piece of cartilaginous nasal septum was in normal position. A defect 1.5 cm. in diameter in the skin of the nose was a ragged shallow ulcer which had a granular yellow base. Section showed a firm white tumor beneath the ulcer and adjacent epidermis. Microscopically, the skin showed atrophic changes and absence of appendages similar to that seen in irradiation effect. The tumor replaced much of the corium and, in one area, the proliferating fibrous tissue of the tumor was continuous with the perichondrium of the nasal septum. The pathologic diagnosis was postirradiation fibrosarcoma.

Case 3. W. R., an 81 year old white man was admitted to the hospital July 31, 1955. Three years before he had received irradiation by interstitial radium needles (2617 mg. hr.) to the lower lip which was completely filled with a squamous cell carcinoma. Most of the lower lip was absent after the treatment, healing having taken place in a few months. The exposed gum had caused trouble and his complaints were related to drooling and inability to speak clearly. One year after the treatment, a little growth was noted on the gum near the midline. This continued to enlarge slowly until the time of this hospital admission.

Examination showed a moderately obese white man with bilateral ectropions of senile type with lacrimation. An exophytic mass 3 by 2 cm. was present on the gingiva near the midline of the edentulous mandible. The lower lip was missing except for a very small portion, less than 5 mm. in width at both commissures (fig. 7). The mass which was firmly adherent to the mandible but did not extend lingually or more than one-half way down the mandible in depth, was moderately firm, yellowish-pink, and was covered with a thin membrane over the ulcerated surface. There were no palpable cervical nodes. There were systolic mitral and aortic murmurs, a moderately enlarged prostate gland, and numerous keratoses of the hands, but no other significant findings.

Laboratory examination showed normal findings for complete blood count, urinalysis, and serology. The nonprotein nitrogen was 45.6 mg. per cent. An electrocardiogram demonstrated an essentially normal tracing. Roentgenologic examination of the chest showed some aortic calcification but the mandible was normal.

At operation on August 4, wide excision of the mass on the gingiva was done, extending 1 cm. lateral to its palpable margin. The mass was thought to be recurrent carcinoma. With

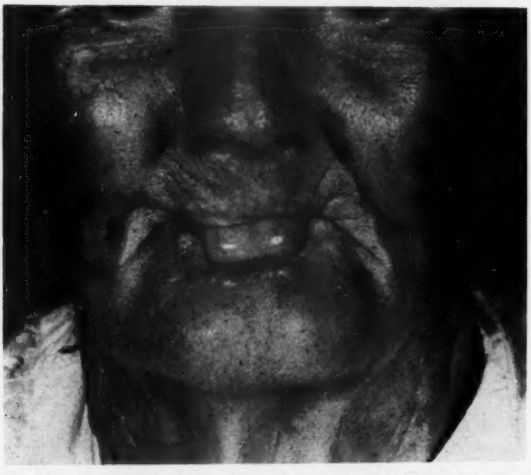

FIG. 7. Case 3. Absence of lower lip almost complete in 81 year old man who had had interstitial radium therapy for carcinoma. The mass on the gum is obscured by the tongue but does show slightly at the bottom of the defect just to the left of the midline.

FIG. 8. Case 3. Early appearance postoperatively after reconstruction of lower lip.

FIG. 9. Case 3. Lateral view of lip reconstruction

an Albee saw the mandible was cut horizontally to excise the superior one-half of the thickness of the bone. No involvement of the bone was seen at the line of excision. Reconstruction of the lip was made by the method of Dieffenbach. Three submental nodes were removed at the time. The result has been most gratifying to the patient from the functional standpoint and the appearance is satisfactory (figs. 8, 9).

Pathologic Findings. The specimen consisted of the lower lip, central part of the mandible, and submental tissue in which lymph nodes were present. The lip and skin from the chin measured 4.5 by 5.5 by 2.5 cm., and was of a "*Y*" shape, due to ulceration and loss of much of the central part of the lip. The ulcerated border of the lip was below the level

of the edentulous mandible. The skin near the ulcer was white and slightly elevated at the ulcer edge. The ulcer was 3 cm. in length. The bed of the ulcer was brown, and on section a firm grey zone, .2 to .5 cm. in thickness, underlay the ulcer and was adherent to the anterior surface of the mandible. The 4 lymph nodes found were homogeneous, the largest being .6 cm. in its greatest diameter. Microscopically, the skin showed only moderate irradiation changes; however, the vessels below the ulcer showed marked reduction in the size of the lumina. Much of the ulcer had a thin zone of chronic granulation tissue, whereas the thicker grey zone noted in the gross was composed of a low grade fibrosarcoma. The periosteum of the mandible was continuous with the proliferating stromal elements of the sarcoma. The marrow spaces of the mandible were filled by fibrous tissue. The lymph nodes did not contain tumor. The pathologic diagnosis was postirradiation fibrosarcoma.

DISCUSSION

Connective tissue shows a response to irradiation that is not typical or unique but a change that could be the result of trauma, chronic inflammation, or physical stimulus. Stout[6] stated that there is an "inherent tendency in the affected individual to develop exaggerated fibroblastic proliferation. Such an effect is sometimes induced in an individual as the result of excessive irradiation". Dense collagen bundles with interlacing reticulin fibers between the cells are seen in simple proliferative fibromatosis but they are more pronounced in the fibrosarcomas which show bizarre nuclear forms with cellular irregularity, hyperchromatism, and pleomorphism. The chief criterion of malignancy is infiltrative growth.[4] All of our 3 patients showed direct extension of the fibrous overgrowth into and around normal structures, substantiating the opinion that they were fibrosarcoma.

Metastases occurred in only 25 per cent of 206 cases of fibrosarcoma reviewed by Stout.[4] They were much more rarely found in these tumors that follow irradiation but can occur in viscera and lymph nodes.[5] Epidermoid carcinoma and fibrosarcoma have been reported together in irradiated[3, 5, 7, 8] tissue as is shown in case 1 (fig. 5). Some difficulty may be encountered at times in regard to the interpretation of the tumor as fibrosarcoma or a spindle cell variant of epidermoid carcinoma, but the connective tissue origin of the tumor usually is a clue to the correct interpretation. Most of the changes reported are in the skin but some fibrosarcomas following irradiation have been reported in the tongue, liver,[2] and bone.[1]

The inciting cause in these patients often is roentgen therapy given in small dosage repeatedly over a period of several months or even years for a relatively benign condition such as hypertrichosis, keloid, lupus vulgaris, thyroid disease, or tuberculous arthritis. One early report[3] shows the stimulus to be repeated fluoroscopic exposure to the hands of a doctor. Deep and heavy dosage to treat squamous cell carcinoma or other epithelial new growth has *"cured"* the primary lesion[4] only to have malignant changes appear much later as the result of the radiation given. A long latent period, as long as 27 years in 1 reported case,[4] may exist between exposure and the patient's awareness of the difficulty; over five years is the rule. The presence of chronic inflammation in the connective tissue and the addition of irradiation as shown experimentally (Lacassagne and Vinzent, cited by Hatcher[1]) may demonstrate a cause and effect relationship in

the production of fibrosarcoma, but irradiation alone will produce the same change.

Treatment of masses in irradiated tissue developing years after the exposure should be relatively radical. Local excision should be wide and complete without initial consideration being given to closure. Stout[6] believed that a margin of excision of 2.5 cm. out into good tissue away from the peripheral palpable confines of the mass is necessary. In the face or hand, such wide excision would not seem to be practical but the point should be made that the removal must be wide to be adequate. Regional nodes need not be removed prophylactically as they are so rarely involved.

SUMMARY

Fibrosarcoma, although rare, can occur as the result of irradiation. It usually occurs in or around the skin years after improper irradiation, given originally for a benign condition for which such therapy usually is not indicated. Fibromatosis only is present early but when local invasion occurs the tumor should be classified as malignant even though metastases are very rare. Wide local excision is indicated. The cases of 3 patients with irradiation fibrosarcoma, 1 with coexisting basal cell carcinoma, are reported for the purpose of making better known this entity.

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COMPETENCE OF THE ESOPHAGOGASTRIC SPHINCTER IN HIATAL HERNIA: SOME EXPERIMENTAL OBSERVATIONS*

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There continues to be some speculation concerning the relative importance of the diaphragm as a factor permitting or preventing reflux of gastric secretions into the esophagus. Continence in the esophagogastric area has been reported to be attributable to a number of factors, some of which are the diaphragm and its "*pinchcock*",[23, 26] the crura of the diaphragm,[6] the inferior constrictor of the esophagus,[16] the angle of entrance of the esophagus into the stomach,[3] and the esophagogastric valve[11, 17] or sphincter.[3, 10] The esophagogastric junction is said to contain no anatomic sphincter, grossly or microscopically, yet there is at that point a well defined division of structures which differ greatly in appearance and function. For example, the mucosa of the esophagus, highly susceptible to the injurious action of the secretions of the gastric mucosa, normally adjoins that mucosa with safety because of some protective mechanism not yet anatomically defined. Although the transport of material through this area is predominantly in one direction, this junction of esophagus and stomach appears to be more than a physical valve in that it probably is capable of active as well as passive movement.[10]

That the junction probably contains a functional sphincter is further suggested if the clinical condition of cardiospasm (achalasia, dystonia) is considered. The esophagogastric junction in patients with cardiospasm intermittently impedes the normal flow of swallowed material into the stomach. Esophagitis in untreated patients with cardiospasm is rare, indicating marked or exaggerated continence, if you will.

Antithetically, the esophagogastric junction may be abnormally patulous as in cases of chalasia in infants.[5] Incompetence of the esophagogastric junction is extreme in these patients and sustenance, with improvement of symptoms, depends on the infant's eating and swallowing in an upright position.

Incontinence at the esophagogastric area, with reflux esophagitis, occurs occasionally with obstructing duodenal ulcers and with hiatal hernias.[4] When the esophagogastric junction is altered surgically (even by means of an inlying gastrointestinal suction tube[18]) reflux esophagitis easily occurs. Esophagitis frequently follows plastic and anastomotic procedures for cardiospasm,[2] and resection operations for carcinoma.[20] With the increasing facility for surgical procedures in the esophagogastric area, from the thoracic approach above and the abdominal route below, there has been a concomitant increase in the incidence and recognition of esophagitis. The complication of esophagitis with its

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sometimes attending ulceration and stricture may be as incapacitating to the patient as the original condition for which operation was done. The potential danger of esophagitis is a serious deterrent to some operations in this crucial area.

Experimentally, reflux esophagitis, presumably due to incompetence of the esophagogastric area, has been produced in a number of ways. Simple pyloric obstruction due to surgical ligation is followed by a high incidence of esophageal erosive lesions.[11, 12] Selye demonstrated that the addition of another ligature at the cardia prevented the esophagitis following pyloric ligation in the rat.[21] When the esophagogastric sphincter is excised in the dog and restoration of gastrointestinal continuity is effected by esophagogastrostomy, even with extensive upper gastrectomy, esophagitis is a constant sequela.[15] This circumstance prompted Dillard and Merendino to interpose a segment of jejunum between the esophagus and stomach in order to prevent esophagitis in dogs,[9] and with various excisional procedures, in man.[19] Clatworthy also has demonstrated the protective capacity of interposed intestinal segments.[22] That the esophagus is sensitive to erosion by both acid and alkaline secretions has been demonstrated,[1, 7] and gastric resection has been advocated for the reduction of gastric secretions in cases of esophagitis with stricture.[24] Surgically constructed valves have been fashioned to provide a measure of protection of the esophagus from gastric secretions.[8, 25] Regurgitant esophagitis was shown to occur regularly when hiatal hernia was produced in dogs by excision of the left crus of the diaphragm, a study which stressed the importance of the diaphragmatic "*pinch-cock*" mechanism in the dog.[14]

The remarkable ability of a normal esophagogastric junction to protect against esophagitis and even reverse an already established esophagitis in dogs with esophagogastrostomy has been demonstrated.[13] These observations prompted the following investigations to further isolate the anatomic area wherein continence lies and to study certain factors influencing the competence of the esophagogastric sphincter.

EXPERIMENTS

Adult mongrel dogs were used throughout the study. Three groups of experiments are reported here, which have for their purpose the isolation of the functional sphincter and the delineation of some of the conditions which alter the function of the sphincter with respect to the clinical problem of hiatus hernia. In Group A the experiments were devised so that the intrinsic factor and the diaphragmatic factor of esophagogastric competence could be separated for determination of their relative importance in the dog. In Group B the influence of intragastric pressures on the competence of the esophagogastric sphincter in the dog was studied. In Group C the effect of varying degrees of gastric obstruction at the level of the diaphragm upon sphincteric competence in experimental hiatus hernia was observed. In Groups A and C incompetence of the sphincter was assumed when esophagitis due to erosion from gastric chyme was present. In Group B incontinence was visualized and objectively determined.

In all groups operations, using aseptic precautions, were done under intravenous pentobarbital anesthesia (15 mg. per pound body weight) with endo-

tracheal oxygen administration. The left transthoracic approach to the esophagus was used. Hemostatic ligatures and sutures were of fine black silk. Parenteral fluids and antibiotics were used postoperatively until food and fluids were tolerated by the animal. Gastric analyses for free hydrochloric acid with histamine stimulation were done preoperatively and postoperatively. The dogs were weighed at regular intervals and, at the completion of study, were killed under anesthesia for gross and microscopic examination of tissues, particularly the esophagus and cardiac sphincter.

Group A. Isolation of the Functional Sphincter at the Esophagogastric Junction

Methods: Dogs in this group were divided into 3 series of experiments. In all dogs the thoracic esophagus was divided 3 cm. above the diaphragm with closure of the distal segment and anastomosis of the proximal segment to the fundus of the stomach, which was drawn through an incision in the dome of the diaphragm. Esophagogastric continuity thus by-passes the esophagogastric junction. The position of the distal esophageal stump in relation to the diaphragm was varied in the 3 series of dogs. Observations were made of both the distal esophageal stump in its varied positions and the esophagus above the esophagogastrostomy, at the completion of the experiments.

Results: Series I (table I): In this series (fig. 1) 9 dogs had esophagogastric anastomosis with the distal esophageal stump remaining in its normal position above the diaphragm. None of the 9 dogs developed any abnormality of the distal esophageal stump when it was left in its normal position above the diaphragm (fig. 2). The esophageal mucosa was protected by either the esophagogastric sphincter or the diaphragm, or both. Eight of the 9 dogs developed esophagitis in the control area—above the esophagogastrostomy.

TABLE I

Group A: Dogs with esophagogastrostomy

Series I: Distal esophageal stump in normal position

Dog No.	Gastric Acidity (Degrees Free HCl)	Days	Findings		Remarks
			Esophageal stump	Esophagus above anastomosis	
119	60	14	Normal	No esophagitis	Died of empyema due to surgical contamination
120	100	20	Normal	Severe esophagitis with perforation	Vomiting, weight loss
115	—	29	Normal	Moderate esophagitis	Vomiting, weight loss
43	12	64	Normal	Mild esophagitis	Occasional vomiting
47	74	65	Normal	Moderate esophagitis	Slight anastomotic stenosis
114	70	76	Normal	Moderate esophagitis	Occasional vomiting
118	24	77	Normal	Moderate esophagitis	Occasional vomiting
113	0 (no hist.)	78	Normal	Moderate esophagitis	Moderate anastomotic stenosis
117	55	82	Normal	Moderate esophagitis	Occasional vomiting

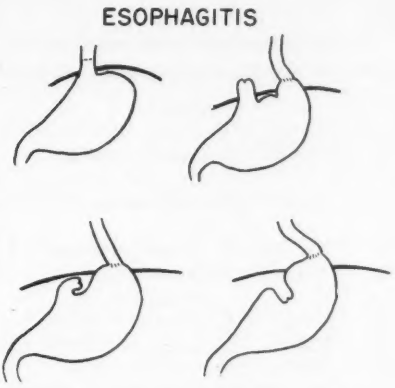

FIG. 1. Diagram of Experimental Preparations for Group A Experiments. Upper left: Shows level of division terminal esophagus in all dogs. Upper right: Series I. Esophagogastrostomy and distal esophageal stump in normal position. Lower left: Series II. Esophagogastrostomy and distal esophageal stump placed under diaphragm. Lower right: Series III. Esophagogastrostomy and distal esophageal stump inverted into gastric lumen.

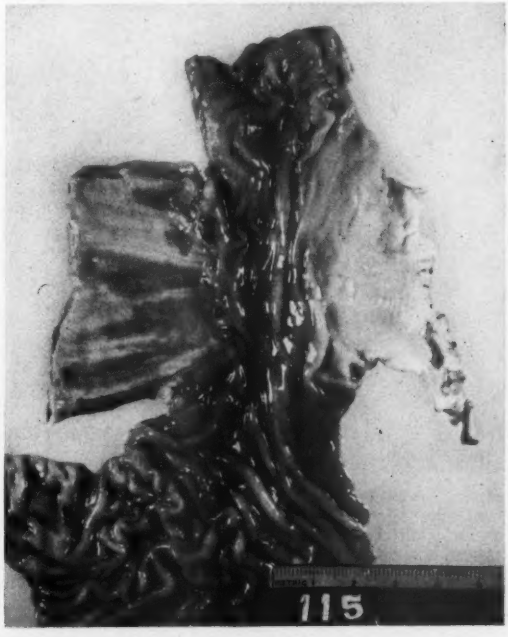

FIG. 2. Photograph of specimen of stomach and esophagus of dog no. 115 (Series I). The esophagus at the left shows esophagitis above the esophagogastrostomy, while the distal esophageal stump on the right is normal.

TABLE II

Group A: Dogs with esophagogastrostomy

Series II: Distal esophageal stump placed under diaphragm

Dog No.	Gastric Acidity (Degrees Free HCl)	Days	Findings		Remarks
			Esophageal stump	Esophagus above anastomosis	
15	74	6	Normal	Moderate esophagitis	Empyema due to surgical contamination
19	94	28	Normal	Esophageal erosions	Anorexia, weight loss
76	—	39	Normal	Severe ulcerative esophagitis	Anorexia, weight loss
52	93	68	Normal	Esophagitis	Intermittent vomiting
124	80	68	Normal	Moderate esophagitis	Infrequent vomiting
14	50	79	Normal	Severe esophagitis	Ulceration of esophagus

FIG. 3. Photograph of specimen of stomach and esophagus of dog no. 15 (Series II). The esophagus at the top shows severe esophagitis above the esophagogastrostomy while the distal esophageal stump (bottom of picture) is normal. The esophageal stump was placed beneath the diaphragm, and protected only by the esophagogastric sphincter.

Series II (table II): In this series (fig. 1) 6 dogs had esophagogastric anastomosis with the closed distal esophageal stump placed just below the diaphragm with suture closure of the diaphragmatic hiatus. In none of the 6 dogs was there esophagitis of the distal esophageal stump when it was placed below the diaphragm (but still above the cardia of the stomach) (fig. 3). The esophageal

TABLE III

Group A: Dogs with esophagogastrostomy

Series III: Distal esophageal stump inverted into gastric lumen

Dog No.	Gastric Acidity (Degrees FreeHCl)	Days	Findings		Remarks
			Esophageal stump	Esophagus above anastomosis	
75	60	5	Severe esophagitis	Normal	Died early of atelectasis
16	94	6	Severe ulcerative esophagitis	Normal	Died of empyema due to surgical contamination
23	76	9	Bleeding ulcerative esophagitis	Severe esophagitis with ulceration and perforation	Empyema due to esophageal perforation
20 (1)	15	34	Ulcerative esophagitis; small stump	Moderate esophagitis	Occasional vomiting; weight loss
20 (2)	60	39	Ulcerative esophagitis; small stump	Moderate esophagitis	Intermittent vomiting
77	0	71	Mucosa of stump replaced by scar	Severe esophagitis with ulceration	Gradual weight loss
122	0	75	Stump replaced by scar	Severe esophagitis with ulceration and scarring	Occasional vomiting; gradual weight loss

mucosa was protected by the esophagogastric sphincter without the aid of the diaphragm. Esophagitis developed in the control area (above the esophagogastrostomy) in each dog.

Series III (table III): In this series (fig. 1) 7 dogs had the usual esophagogastric anastomosis with the closed distal esophagus not only inverted under the diaphragm but also inverted into the stomach lumen, with hiatal closure. In each of the 7 dogs in this series there was esophagitis with severe ulceration of the distal esophageal stump when it was placed under the diaphragm and inverted into the stomach lumen (fig. 4). The esophageal mucosa was not protected by either the sphincter or the diaphragm. Esophagitis was present also in the control area above the esophagogastrostomy in all dogs except 2, one of which died on the fifth day and one on the sixth day following surgery. Each of these 2 dogs dying early had developed by this time severe ulceration of the inverted esophageal stump which had been constantly bathed in gastric juice. After the early ulceration which develops in the inverted esophageal stump there is a contraction of this stump with continuing ulceration until all the esophageal mucosa is lost and replaced by scar tissue, as noted in dog no. 77, killed 71 days after operation, and in dog no. 122, killed 75 days after operation.

Nineteen of the 22 dogs in the 3 series developed esophagitis above the esophagogastric anastomosis; esophageal lesions developed in the distal esophageal stump only when the cardiac sphincter was defunctionalized.

FIG. 4. Photograph of specimen of stomach and esophagus of dog no. 23 (Series III). The esophagus at the top demonstrates severe ulcerative esophagitis with perforation above the esophagogastrostomy. The distal esophageal stump which had been inverted into the gastric lumen to defunctionalize both the intrinsic sphincter and the diaphragm shows severe bleeding esophagitis.

Group B. The Influence of Intragastric Pressure Changes on the Competence of the Esophagogastric Sphincter

Method: Five dogs were used in this group of experiments. Through an upper midline abdominal incision the pylorus was completely obstructed by a heavy ligature of umbilical tape. A gastrostomy of the Stamm type was placed in the distal half of the anterior surface of the stomach for the purpose of installation, under measured pressure (mercury manometer), of sterile water containing Evans blue dye. A rigid plastic catheter (no. 10 French) also was placed into the central portion of the stomach by gastrostomy and connected to a Statham pressure transducer for measurement of intraluminal gastric pressures on a Poly Viso multiple-channel recorder (fig. 5). Both tubes were led out of the abdomen through the closed abdominal incision. When it was desired to measure the intraesophageal pressure a similar plastic catheter was placed through the mouth of the dog so that the end of the catheter was located in the terminal thoracic esophagus above the diaphragm. This tube also was used to denote the entrance of the blue colored fluid into the esophagus from the stomach. In 3 of the dogs, through a short left thoracic incision, the terminal esophagus was opened to confirm the presence and time of reflux of the blue fluid into the esophagus through the sphincter from the stomach. The effect of the closed

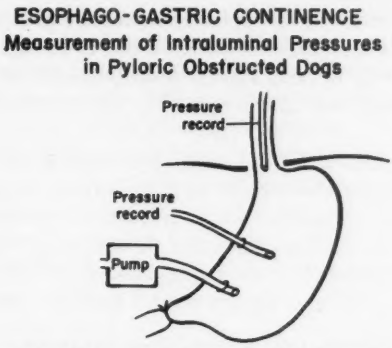

FIG. 5. Diagram of experimental preparation for measurement of intraluminal pressures. Fluid containing blue dye is pumped into stomach above the ligated pylorus. Incontinence is determined by pressure recordings and by noting appearance of blue dye in esophagus.

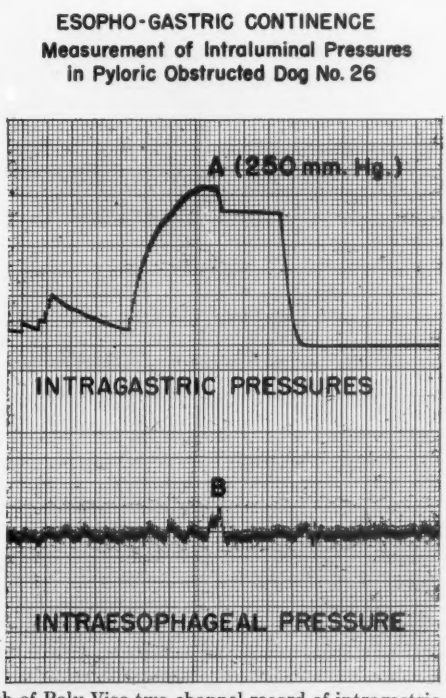

FIG. 6. Photograph of Poly Viso two-channel record of intragastric and intraesophageal changes in dog no. 26. With a rapid installation of blue colored fluid into the stomach, the pressure rises from an average of 6 mm. Hg to 250 mm. Hg at which point (A) there is a sudden decrease in pressure concomitant with transient elevation (B) of esophageal pressure. At this time there is visible reflux of the blue material into the esophagus and the intragastric pressure falls to zero with continued incontinence at the esophagogastric junction. The pylorus is ligated in the anesthetized dog.

and of the open thoracic cavity upon intraluminal pressures was noted and taken into consideration in these studies. In one of these dogs a hiatal hernia was constructed (Group C) and intraluminal pressures of the stomach, both infradiaphragmatic and supradiaphragmatic, and of the esophagus were remeasured.

Results: Increased pressure in the stomach is capable of *"breaking"* the competence of the esophagogastric sphincter if it is either sudden and forceful or gradual and persistent. A sudden rise in intragastric pressure to 250 mm. Hg within 1 minute causes a sudden release of fluid through the sphincter into the esophagus (fig. 6). Immediately following this, although the pressure in the stomach falls to 0.0 to 6.0 mm. Hg (its normal level in these studies) there con-

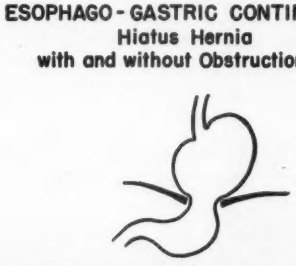

FIG. 7. Diagram of the experimental preparation in Group C experiments. The esophageal attachments at the diaphragmatic hiatus are divided and the stomach, with its esophagogastric sphincter, is drawn up into the chest. The diaphragm is sutured about the body of the stomach to produce varying degrees of obstruction.

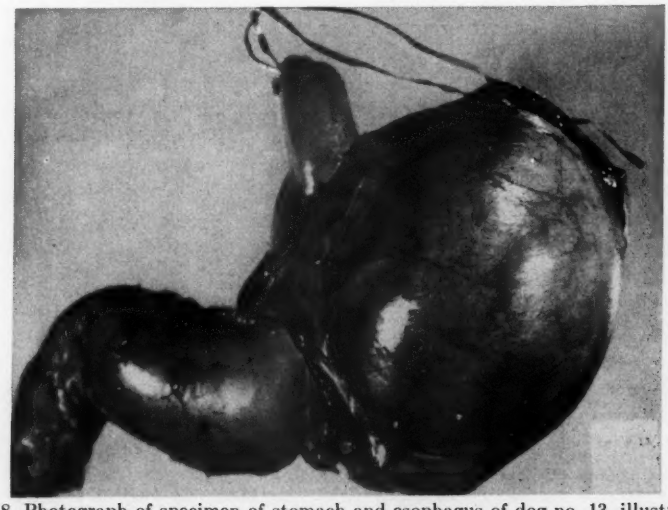

FIG. 8. Photograph of specimen of stomach and esophagus of dog no. 13, illustrating a moderate degree of obstruction at the diaphragm of this intact hiatal hernia at the time of sacrifice (shortly after the animal had eaten). Before excision of this specimen the esophagus (top of picture) was not distended. There was no esophagitis or gastric erosion with this moderate obstruction.

tinues to be incontinence and reflux. Continence does not return during 1 hour of observation following sudden failure of continence due to sudden elevation of gastric pressure. When the intragastric pressure is elevated slowly, the stomach enlarges greatly, containing about 1500 cc. of injected fluid at 150 mm. Hg before incontinence is manifest by observation of the blue dye in the lower esophagus. When this method is used the intragastric pressure can be raised and lowered successively to demonstrate the pressure of incontinence as around 150 to 160 mm. Hg. The resting pressures in the stomach were approximately 6 mm. Hg; in the esophagus they were +4 to −2 mm. Hg, depending upon the respiratory phase. The pressure in the thoracic portion of the stomach in a hiatal hernia is similar to the intraesophageal pressures.

Group C. The Effect of Obstruction on Sphincteric Competence in Hiatus Hernia

Method: Hiatal hernias were surgically created in 14 dogs. Through a left transthoracic approach the attachments of the esophagogastric junction to the diaphragm were divided meticulously and the stomach with the esophagogastric

FIG. 9. Photograph of specimen of stomach and esophagus from dog no. 78-1. There is linear esophagitis with gastric erosions above a severe obstruction at the diaphragm in this hiatal hernia. The severe degree of obstruction caused incontinence of the esophagogastric area with reflux esophagitis.

junction was drawn up into the left chest for a distance of 6 to 10 cm. The esophageal hiatus then was sutured about the body of the stomach with interrupted no. 000 black silk, varying the size of the hiatus and, indirectly, the degree of obstruction of the stomach at the diaphragm (fig. 7). The thorax was closed and the dogs cared for as previously described. Observations as to weight, ability to eat, and incidence of vomiting were recorded prior to killing the dogs, which was done from 4 to 96 days after operation. The presence or absence of esophageal and gastric lesions and the degree of mechanical obstruction were recorded at the termination of the study.

Results: As is noted in table IV, esophagogastric lesions in experimental hiatal hernias do not occur even though there is upward displacement of the sphincter and the upper stomach from the diaphragm unless there is a serious degree of obstruction distal to the sphincter. Even though the size of the thoracic stomach and the displacement of the sphincter was great in most of the dogs there was no incontinence unless mechanical impediment at the diaphragm was extreme. When gastric ulceration was present it was uniformly at the level of the diaphragmatic constriction.

Purposeful production of varying degrees of obstruction at the hiatus is not predictable. When the esophagodiaphragmatic membrane is incised there is immediate widening of the hiatus. Furthermore, reconstruction of the hiatus about the greatest diameter of the stomach is not certain to produce obstruction because, in the dog, the crura are muscular, not tendinous.

TABLE IV

Group C: Dogs with experimental hiatus hernia

Dog No.	Gastric Acidity (Degrees Free HCl)	Days	Degree of Obstruction*	Findings
11	—	31	None	No esophagitis
2	80	37	None	No esophagitis
9	—	63	None	No esophagitis
1	80	72	None	No esophagitis
105	6	75	None	No esophagitis
13	52	78	Moderate	No esophagitis
3	92	84	Moderate	No esophagitis
35	80	89	Moderate	No esophagitis (small gastric erosions at diaphragm)
46	88	96	Moderate	No esophagitis
21	50	68	Moderate	No esophagitis
102	68	78	Moderate	No esophagitis
142	74	85	Moderate	No esophagitis
78 (1)	75	4	Severe	Severe ulcerative esophagitis; two small ulcerations at diaphragm
78 (2)	60	22	Severe	Esophageal erosions; gastric ulceration

* None = Diaphragmatic hiatus admits 3–4 fingers at time of sacrifice. Moderate = Diaphragmatic hiatus admits 2 fingers at time of sacrifice. Severe = Diaphragmatic hiatus admits only 1 finger at time of sacrifice.

The esophagus, shortened in the chest of dogs with hiatal hernia, could be drawn down easily into the abdomen, even several months after operation.

DISCUSSION

From these few observations it is evident that the esophagogastric sphincter in dogs, although not described anatomically, is competent under experimental conditions until rather severe and extreme stresses are placed upon it. High intragastric pressures with pyloric obstruction are capable of finally producing incontinence, measured and seen as reflux into the esophagus. Only with an extreme degree of obstruction at the diaphragmatic level in hiatal hernia does there occur incontinence and reflux esophagitis. The diaphragm, eliminated as a factor of continence in the Group A experiments, does not participate in the development of esophagitis (or sphincteric incompetence) in hiatal hernia, except indirectly in the occasional instances when it causes severe gastric obstruction. In this respect the obstructing diaphragm plays a part similar to the obstructing duodenal ulcer in the predisposition to secondary reflux esophagitis. Similarly in the dog, the ulcer diathesis could have been reproduced by means of chronic histamine-in-beeswax administration, which most likely would have increased the severity if not the incidence of esophagitis in the presence of obstructing hiatal hernia.

In the Group A experiments it is noted that 3 dogs (nos. 119, 75 and 16) did not develop esophagitis above the esophagogastrostomy; this fact probably is accountable to the circumstance that insufficient time had elapsed for erosion. Others have reported that the incidence of esophagitis above an esophagogastrostomy is 100 per cent if chronic histamine-in-beeswax stimulation is added.

In those dogs in which the distal esophageal stump was inverted into the gastric lumen, obviating both diaphragm and esophagogastric sphincter, esophagitis developed early because of constant contact of the esophagus with gastric secretions. It is believed that constriction of the blood supply is not a factor. The mucosa of the inverted esophagus finally is destroyed and replaced by scar tissue. This severe and early degree of involvement does not occur above an esophagogastrostomy, probably because the contact of the esophageal mucosa with gastric secretions is only intermittent.

The studies of the influence of intragastric pressure upon the sphincter are interesting although not complete. It appears that prolonged sustained pressure may open the sphincter at a lower pressure (150 to 160 mm. Hg) than when the pressure is raised precipitously (250 mm. Hg). There follows a temporary incompetence, at least, of the sphincter which does not resist even normal gastric pressures. This incompetence probably is only temporary since examination of the esophagus 42 and 56 days later, when 2 such animals were killed, did not show any evidence of reflux esophagitis. It should be pointed out that the pressure studies were done in anesthetized dogs, on their backs, under experimental conditions. In these dogs, the stomach under pressure was atonic and large and exhibited no peristaltic activity. Abdominal muscle activity, probably more important in raising intragastric pressure (as seen in vomiting or straining) also

was diminished in these dogs. Experimental pyloric obstruction also was present in the dogs. Nevertheless, the intragastric pressures during vomiting and other forceful activity probably rise to levels comparable to the values produced in these experimental animals.

The type of hiatal hernia produced in the dogs in these experiments is of the sliding variety. The esophagus thus was necessarily short, by virtue of its contractibility. There was no kinking or circuitous course of the esophagus. At the time of sacrifice the stomach and esophagus could be pulled easily into the abdomen without undue tension, except in the dogs with severe obstruction and resultant severe esophagitis. Clinically, the esophagus in hiatal hernias of the sliding type, often considered to be congenitally short, may be short only because of its own contractibility, or in some cases short and inelastic when esophagitis due to reflux of gastric secretions has occurred.

In the experimental dog, the diaphragmatic *"pinch-cock"* does not appear to exist, as these experiments strongly indicate that the diaphragm is not active in esophagogastric continence. Diaphragmatic hernias may be due to an inherent or to an acquired weakness of the phrenico-esophageal membrane or diaphragmatic musculature, but the complication of esophagitis is dependent primarily upon the competence of the esophagogastric sphincter, separable from the diaphragm. Gastric obstruction at the diaphragm may, if severe, render the sphincter incompetent.

CONCLUSIONS

Continence of the esophagogastric junction of the dog is dependent primarily upon the intrinsic esophagogastric sphincter, and is in no way dependent upon its normal diaphragmatic attachments.

The esophagogastric sphincter of the dog is remarkably competent. Under the conditions of the reported experiments intragastric pressures of 150 to 250 mm. Hg were nesessary to produce incontinence at the esophagogastric area with reflux into the esophagus.

Reflux esophagitis does not develop in dogs with experimental hiatal hernia unless the degree of gastric obstruction at the level of the diaphragm is great, in which case the sphincter above the obstruction probably is rendered incompetent.

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FEMINIZING TUMORS OF THE ADRENAL CORTEX*

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Feminizing changes consisting of enlargement of the breasts, a decrease in testicular size and impotence occurring in a 26 year old man having a carcinoma of the adrenal cortex was described by Bittorf[2] in 1919. A thorough review reveals that only 27 such cases have been reported in the world literature. To this group we are adding a case, the first ever reported in a Negro, and are tabulating the collected findings in the previously reported cases.

Since the adrenal cortex is an exceedingly complex organ, it is not surprising that tumors of this gland may produce a wide variety of clinical changes. Although some cortical tumors produce no generalized endocrine manifestation, most patients with such lesions present dramatic and striking changes depending on the predominant hormones elaborated by the tumor as well as the age and sex of the individual concerned.

Broadly speaking, the signs and symptoms produced by these lesions can be divided into two large categories (1) those associated with metabolic alterations (Cushing's syndrome) and (2) those with sexual changes (adrenogenital syndrome), although it must be emphasized that considerable overlapping of the two groups exists in many cases. The classical findings of obesity, osteoporosis, hypertension, muscular weakness, polycythemia, skin striae and acneform eruptions in Cushing's syndrome are well known. In the second category the sexual changes predominate and overshadow the metabolic manifestations. In the prepubertal child, cortical tumors generally present a picture of rapid aging, resulting in the so called "infant Hercules" in the male or the development of sexual precocity, hirsutism, enlargement of the genitalia and a deepening of the voice in female children. In the adult female the hormonal secreting tumors produce a general tendency toward virilism characterized by marked facial hirsutism, masculine fat distribution, suppression of menses, loss of libido and enlargement of the clitoris. These changes are much less common than are those of Cushing's syndrome although many instances of an overlapping of the two groups of changes occur. In the adult male feminizing changes characterized by gynecomastia,[13, 28] loss of libido and a decrease in testicular size are extremely rare as previously stated. It is with this group of patients that this paper is concerned.

CASE REPORT

A. J. W. a 26 year old Negro man, was admitted to the Kansas City Veterans Administration hospital on July 8, 1954 because of painless swelling of the right breast. The left breast

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had been removed surgically in September of 1949 at another hospital. The patient stated that he had been essentially well until February of 1954, 5 months prior to admission, when he first noticed pain in the right scapular region and aching pains in the right lumbar area. The pain increased in severity until April 1954 when he consulted a private physician who found him to be anemic and prescribed iron. By June the pain had become increasingly severe and had localized in the right hypochondrium and right lumbar region. The size of the right breast had been gradually increasing for approximately 9 months prior to admission. The breast was tender to touch but otherwise not painful. There had been no milk or other secretion from the breast. Further questioning revealed that the patient had noticed inability to ejaculate during intercourse for approximately 12 months prior to admission. There had been no loss of libido or erection ability. There also had been noted a decrease in size of the penis and testicles. During the months prior to admission there had been increasing fatigability and a weight loss of 35 lbs. during the 3 months immediately prior to admission. The patient stated that he had been obese as a child, weighing as much as 210 lbs. before the age of puberty. The breasts always had been somewhat larger than average, but had been attributed to the patient's obesity. In 1949 the left breast had been excised because of pain and swelling in the breast. It was stated that his disability developed following a human bite. Pathologic diagnosis of the excised left breast was gynecomastia. During hospitalization in 1949, he was found to have a mild hypertension, the blood pressure being 170/90.

Physical examination showed a well developed, well nourished Negro man with no evidence of acute or chronic illness. The blood pressure was 140/80. The right breast was considerably enlarged, measuring 11.5 cm. in diameter at its base and protruding 6.5 cm. The areola was 3.3 cm. in diameter (fig. 1). The breast tissue was firm and homogeneous, there being no nodularity noted. There was a well healed scar in the area where the left breast had been removed previously. Other physical findings were essentially normal except for mild tenderness in the right hypochondrium and midepigastric region. There were no palpable masses in the abdomen. The testes were smaller than normal.

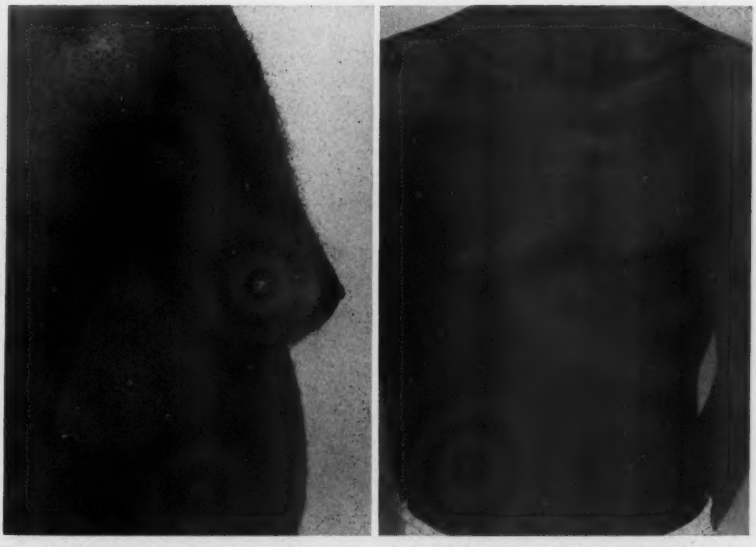

FIG. 1. Photograph showing enlargement of the right breast. The left breast had been removed five years before.

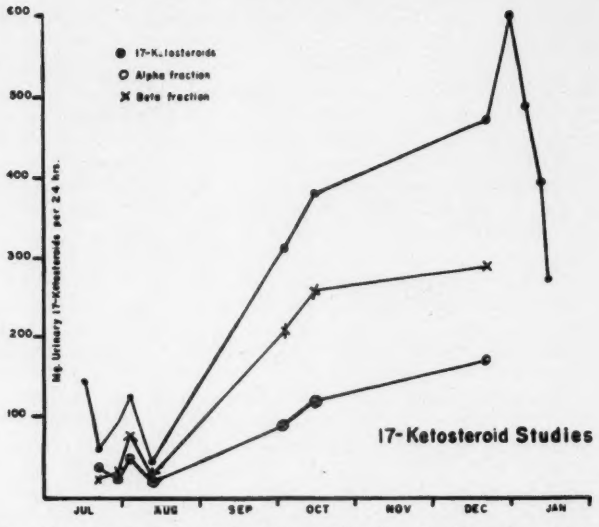

FIG. 2. Graphic record of the 17-ketosteroid levels and the alpha and beta fractions during the 7 months the patient was studied. Note the transient drop following operation August 4.

Laboratory findings showed a hemoglobin of 10.8 gm. Urinalysis was within normal limits. Nonprotein nitrogen and fasting glucose levels were normal. Serum amylase was 133 Somagyi units and the serum lipase was 0.3. The glucose tolerance curve was normal, basal metabolism rate −2, and circulating eosinophile count 63 per cu. mm. Urinary studies of 17-ketosteroid excretion, as well as alpha and beta fractions, are shown in figure 2. The important feature is the extremely high level of 17-ketosteroid excretion, the level rising to 600 mg. per 24 hours as compared with the normal level of 15 mg. Also there is an increase of the beta fraction to approximately 60 per cent as opposed to the normal finding of 10 to 15 per cent. The decrease following operation was transitory with a rapid climb as metastases became more extensive. The terminal drop probably is the result of decreased liver function due to massive liver implants. Additional hormonal studies are tabulated in table I. The significant finding is the huge increase in pregnanediol excretion. Roentgenograms of

TABLE I

Additional hormonal studies

Date	11-oxysteroids/24 hrs	FSH	Friedman Quantitative	Estrogen/24 hr.	Pregnandiol/24 hr.
7-14		96 M.U.			
7-29	3.4 mg.				
8-4				2.64 mg.	
8-13				1.57 mg.	
10-15				4.96 mg.	
12-26					86.6 mg.
12-27			10 cc Neg.		
			20 cc Doubtful		
1-3-55				6.24 mg.	621.6 mg.

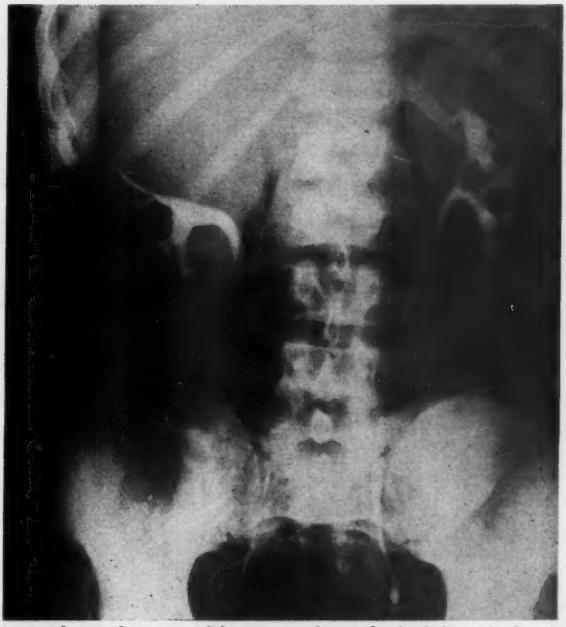

FIG. 3. Retrograde pyelogram with retroperitoneal air injected showing large right suprarenal mass.

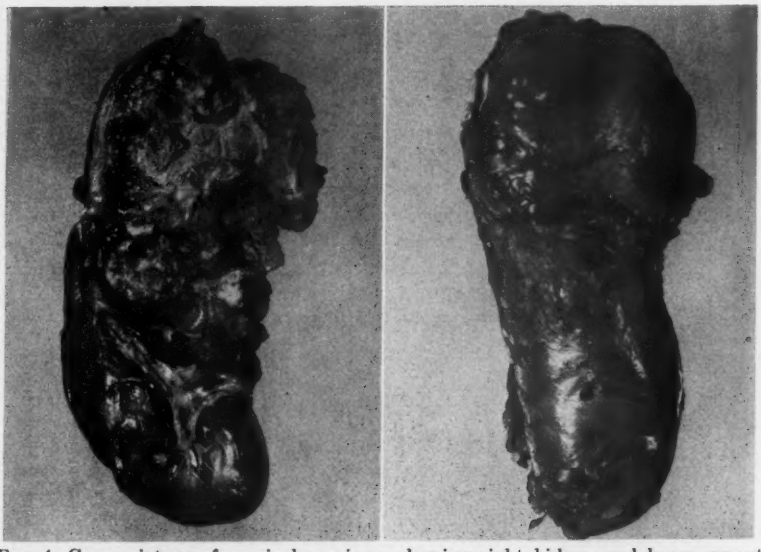

FIG. 4. Gross picture of surgical specimen showing right kidney and large, necrotic suprarenal tumor.

TABLE II

Feminizing adrenal tumors

Clinical features

Case No.	Author	Publication Date	Age	Diagnosis	Breasts				Feminizing Hair Changes	Atrophy of Testes	Atrophy of Penis	Increasing Skin Pigmentation	Acne	Obesity	Palpable Tumor	Blood Pressure	Pain at Tumor	Libido Diminished or Absent	Potency Diminished or Absent
					Gynecomastia	Secretion	Tenderness	Areola pigmente											
1	Bittorf[2] Mathias[13]	1919 1922	26	CA	Yes	—	—	—	No	Yes	—	Yes	—	—	Yes	—	—	—	Yes
2	Parkes Weber[18] Zum Busch[28]	1926 1927	27	CA	Yes	Milky	No	—	—	—	—	—	—	—	—	—	—	—	—
(3)	Holl—Case[7]	1930	15	?CA	Yes	—	—	Yes	Yes	No	No	Yes	—	—	Yes	—	—	—	—
4	Holl—case 2[7]	1930	44	?Adenoma	Yes	—	Yes	Yes	Yes	Yes	Yes	—	Yes	Yes	—	—	—	Yes	Yes
5	Lisser[11]	1936	33	CA	Yes	Watery	No	—	No	—	—	—	—	No	Yes	112/88	Yes	—	—
6	Simpson & Joll[23]	1938	34	CA	Yes	—	—	—	—	Yes	Yes	—	—	Yes	Yes	116/70	Yes	Yes	Yes
7	Pico Estrada[20] Case 1	1940	30	CA	Yes	—	—	—	No	Right	No	Yes	—	No	Yes	120/58	Yes	—	—
8	Pico Estrada[20] Case C	1940	41	CA	Yes	—	—	—	No	No	No	No	—	No	Yes	110/65	Yes	—	—
9	Kooyman[9]	1940	29	CA	Yes	—	—	Yes	Yes	Yes	Yes	No	—	Yes	Yes	130/92	—	Yes	Yes
10	Roholm & Teilum[21]	1942	44	CA	Yes	No	Yes	—	No	Yes	Yes	—	—	No	No	135/85	Yes	Yes	Yes
11	Cahill, Melicow & Darby[3]	1942	53	?	Yes	—	—	—	Yes	Yes	Yes	Yes	—	Yes	No	—	—	Yes	Yes
12	McFadzean[14]	1946	29	CA	Yes	No	No	—	Yes	No	No	—	—	Yes	Yes	120/80	—	Yes	Yes
(13)	Wilkins[26]	1948	5	Adenoma	Yes	No	—	No	—	No	No	—	—	—	No	—	—	—	—
14	Scott & Hudson[22]	1954	42	CA	Yes	No	—	Yes	No	Yes	—	No	—	No	Yes	—	—	No	Yes
15	Armstron[1] Simpson	1948	40	CA	Yes	—	Yes	—	No	No	No	—	—	—	Yes	128/88	Yes	—	—
16	Staffieri, Cames & Cid[24]	1949	25	?Sarcoma	Yes	—	Yes	—	No	No	No	—	—	—	Yes	—	—	—	—
17	Luft & Sjogren[12]	1949	59	Adenoma	Yes	—	Yes	—	No	No	No	Yes	—	No	Yes	180/110	—	—	—
18	Mortensen & Murphy[15]	1951	38	?Adenoma	Yes	No	Yes	—	Yes	Yes	Yes	—	—	No	No	—	—	Yes	—

19	Nusimovish[17]	1952	40	CA	Yes	No	Yes		—	Left	No	No	—	No	Yes	130/90	Yes	Yes	—
20	Pickard et al[19]	1952	14	CA	Yes	No	—	Yes	Yes	Yes	—	—	Yes	Yes	Yes	210/140	Yes	—	—
21	Diczfaulsy & Luft[5]	1952	55	CA	Yes	—	—	—	—	—	—	—	—	—	Yes	—	—	—	—
22	Myhre[16]	1952	34	CA	Yes	No	Yes	—	No	Yes	Yes	—	—	No	Yes	135/95	Yes	Yes	Yes
23	Dohan et al[6] Case 1	1953	30	Adenoma	Yes	—	Yes	—	No	Yes	No	—	—	No	No	200/135	Yes	Yes	—
24	Dohan et al[6] Case 2	1953	58	Adenoma	Yes	—	—	Yes	—	—	—	Yes	—	No	Yes	230/114	—	—	—
25	Curr & Vine[4]	1953	47	CA	Yes	—	—	—	No	Yes	No	—	—	Yes	Yes	140/90	Yes	Yes	—
26	Staubitz et al[25]	1954	38	CA	Yes	—	Yes	—	—	Yes	—	—	—	No	Yes	130/78	Yes	Yes	—
27	Landau et al[10]	1954	28	?Adenoma	Yes	—	—	Yes	Yes	Yes	Yes	—	—	No	No	120/80	No	No	No
28	Case here reported	1956	26	CA	Yes	No	Yes	Yes	No	Yes	Yes	?	No	No	No	140/80	Yes	No	Yes

the chest, spine, gallbladder and gastrointestinal tract were normal. Intravenous urography showed distortion of the calyceal pattern and the right kidney was lower than normal. Retrograde dye studies combined with retroperitoneal air insufflation clearly outlined a large tumor occupying the right upper retroperitoneal area pushing the kidney downward (fig. 3).

Course in Hospital: During the course of studies and without specific treatment, the patient's abdominal pain subsided somewhat. On the basis of the findings, a diagnosis of carcinoma of the right adrenal was made. Numerous transfusions were given preparatory to surgery, but the patient continued to show anemia. On Aug. 4, 1954, under general anesthesia, he was operated upon. The right upper retroperitoneal space was found to be occupied by a large, firm tumor mass measuring approximately 15 cm. in diameter. This was attached to the diaphragm and liver above and to the upper pole of the kidney below. The tumor mass was also intimately adherent to the abdominal vena cava. The tumor, along with the right kidney, was excised although it was impossible to remove the entire tumor due to its attachment to the vena cava above the entrance of the opposite renal vein. The tumor was firmly encapsulated and had a necrotic center (fig. 4). The immediate postoperative course was uneventful. It was decided to administer radiation therapy over the right retroperitoneal area because of the tumor tissue which had been left adherent to the vena cava. Over a period of 25 days 2,010 r units of therapy were administered. During the immediate postoperative period there was noticeable improvement and the patient noted a return of potency. Before completion of this therapy, however, he noticed a painful swelling over the upper end of the right humerus. A roentgenogram of this region showed destructive changes consistent with metastatic carcinoma. Radiation therapy was administered to this region with some improvement in the pain. A chest roentgenogram taken approximately 2 months following operation showed multiple metastatic lesions in both lung fields. On Oct. 26, 1954, the patient was given nitrogen mustard, 6 mg. daily for 4 days, without demonstrable improvement. His general condition showed a fairly rapid decline and he died Jan. 13, 1955. A description of the pathologic features of the surgical specimen and a review of the autopsy findings will be found in the section dealing with pathologic features.

CLINICAL FEATURES

A detailed tabulation of the clinical features of the 27 previously reported cases is found in table II. By definition these cases are all in males and the distinguishing features are concerned with sexual changes toward feminization, although the degree and nature of these changes vary in individual cases.

Age: The age range in the individuals studied was from 5 to 59 years. Twenty-one (75 per cent) were in the third, fourth and fifth decades, a period ordinarily associated with the greatest virilism in the male, and the average age is somewhat below the usual cancer age span.

Breast Changes: Gynecomastia is the most constant and usually the most striking change reported, being present to some degree in every patient (table III). In 15 patients (53 per cent) gynecomastia was the initial manifestation of of the disease. In several patients breast enlargement did not occur symmetrically, the changes developing to a rather marked degree in one breast before the other. Often the breasts were similar in size and contour to those of a well developed young female. Tenderness of the breasts was noted in 11 patients (39 per cent). and at times this became a prominent feature. The areola was prominent and deeply pigmented in some patients. Secretion from the breasts occurred infrequently, being present in only 2 patients (7 per cent).

Hair: Feminizing hair changes were noted in only 8 patients (28 per cent).

TABLE III

Feminizing adrenal tumors

Presenting manifestation and course

Case No.	Initial Sign or Symptom	Time from Onset until Operation	Time from Onset until Death	Course
1	Gynecomastia	—	11 months	Died of metastatic carcinoma
2	Gynecomastia	—	3 months	Died of extensive carcinoma with metastases
(3)	Tumor of hypochondrium	2 months	8 months	An inoperable tumor present with death occurring of cachexia 6 months later
4	Gynecomastia	22 months	—	All of signs and symptoms reversed and patient well 6 months postoperative
5	Flank pain	—	2 months	Died of extensive carcinoma with metastases
6	Gynecomastia	2 years	4 years	Short postoperative remission; x-ray therapy of no benefit; died 23 months postoperative of metastases
7	Pain in arm	—	About 6 months	Died of carcinoma of adrenal with widespread metastases
8	Chest Pain	—	About 9 months	Died of adrenal cortical carcinoma with pulmonary metastases
9	Gynecomastia	3 years	3 years	Inoperable adrenal cortical carcinoma present with metastases; died day following operation
10	Dyspnea on exertion	—	21 months	Died of adrenal cortical carcinoma with widespread metastases; dyspnea apparently related to pulmonary metastases
11	Hair became finer	—	—	Symptoms present 3 years prior to his admission for study; no operation of follow up available
12	Gynecomastia	18 months	—	Libido & potency returned quickly after removal of adrenal cortical carcinoma; only 43 day follow up postoperatively
(13)	Gynecomastia	4 years	—	Normal growth & development with gradual disappearance of gynecomastia 4 years postoperative
14	Gynecomastia	3 months	9 months	Died 6 months postoperative of adrenal cortical carcinoma
15	Pain below costal margin	6 months	11 months	Inoperable adrenal cortical carcinoma with death occurring 5 months postoperatively
16	Hypoglycemic crisis	2 months	—	All symptoms reversed after 3 months and asymptomatic 2 years postoperatively; postoperatively deep radiotherapy given to tumor area
17	Gynecomastia	5 months	5 months	Died 2 days postoperatively in acute shock following removal of large adrenal cortical adenoma

TABLE III—*Continued*

Case No.	Initial Sign or Symptom	Time from Onset until Operation	Time from Onset until Death	Course
18	Gynecomastia	About 20 months	—	Return of libido after 100 mg. of Perandren was implanted; adrenal cortical tumor was later removed with no evidence of symptoms or metastases 5 month postoperatively
19	Gynecomastia	About 7 months	About 1 year	Inoperable adrenal cortical carcinoma died in cachexia
20	Asthenia	—	About 1 year	Died of adrenal cortical carcinoma with widespread metastases; x-ray therapy of no avail
21	Tumor in upper abdomen and gynecomastia	About 1 year	About 1½ years	Died 8 months after removal of an adrenal cortical adenoma due to a diffuse, spreading adrenal cortical carcinoma
22	Loss of libido	—	7 years	Died of adrenal cortical carcinoma with metastases; testosterone proprionate implanted twice with very little improvement
23	Gynecomastia	3–4 years	—	Gynecomastia disappeared 18 months postoperatively & hypertension had subsided considerably; lack of libido persisted
24	—	—	—	No definite signs or symptoms due to tumor noticed by patient. A probable adrenal cortical adenoma was removed with no change in gynecomastia. Death occurred 6 months postoperatively from an apparently unrelated malignant nerve sheath tumor
25	Gynecomastia	3 years	3 years	Adrenal cortical carcinoma incompletely removed because of fall of blood pressure when handling tumor; died 18 hours postoperatively after sudden deterioration
26	?	About 5 years	—	Adrenal cortical carcinoma removed. Pulmonary metastases present was treated with x-ray with no change. No reversal of signs or symptoms nor any evidence of tumor progression in approximately one year postoperatively
27	Gynecomastia	16 years	—	Adrenal cortical tumor removed. He began to develop his secondary sex characteristics rapidly and the quality and quantity of the spermatozoa in ejaculates improved. Apparently normal at the end of one year
28	Loss of potency	12 months	18 months	Adrenal cortical carcinoma removed. There was temporary improvement and return of potency. He died 6 months postoperatively with extensive carcinomatosis

The changes consisted of a feminine distribution of the suprapubic hair and a thinning of the beard.

Testes: Some degree of bilateral testicular atrophy was found in 15 patients (53 per cent). In some patients the atrophy was rather marked.

Penis: The penis was described as being smaller than normal in 9 patients (32 per cent). The degree of change was apparently never very great.

Skin Changes: Increased pigmentation of the skin was noted in 6 patients (21 per cent). Acne was present in 2 patients (7 per cent). Purplish striations were present in one patient.

Metabolic Changes: Evidence of increased adrenal cortical function such as kyphosis due to osteoporosis of the spine or moon facies were absent, but evidense of altered carbohydrate metabolism was present in two patients. One individual was mildly diabetic, and the other had hypoglycemic crises. Obesity was present in 7 patients (25 per cent).

Palpable Tumor: A palpable tumor was present in 20 patients (71 per cent). It was the initial sign in only 2 patients. The tumor was benign in only 3 of the patients in whom it was palpable.

Blood Pressure Changes: The blood pressure was elevated in 4 patients (14 per cent). In 3 of these patients there were metabolic or skin changes present as described above.

Pain: Pain at the site of the adrenal tumor was present in 13 patients (46 per cent). This symptom usually appeared rather late in the course of the disease and was the initial complaint in only 1 patient. An adrenal cortical carcinoma was found in each patient in whom pain was a symptom except 1. In this patient a large adrenal cortical adenoma was found.

Libido: Diminished or absent libido was present in 12 patients (43 per cent). The decrease usually was gradual and occurred during a period of a few months, but at times the change developed more rapidly.

Potency: A decrease or loss of potency was present in 10 patients (35 per cent). This usually accompanied the diminished or absent libido.

DIAGNOSIS

The diagnosis of a feminizing adrenal tumor can be made from a history and physical findings of feminizing changes substantiated by radiographic demonstration of a suprarenal mass and laboratory evidence of an increase in adrenal cortical activity as shown by an increased urinary excretion of cortical steroid end products.

One of the most consistent features to be found in this series of cases was the long delay between the onset of symptoms and the establishment of a diagnosis (table III). The insidious onset and gradual progression of changes usually result in long delay by the patient in seeking medical advice, and the rarity of this syndrome often causes delay on the part of the physician in establishing a diagnosis.

As previously mentioned the most constant and striking clinical feature found in feminizing adrenal tumors is gynecomastia. Idiopathic gynecomastia or gynecomastia associated with other diseases is of course quite common as com-

pared to gynecomastia resulting from adrenal tumors. However, in a patient with gynecomastia, careful examination for testicular atrophy or softening, and careful palpation for a possible abdominal mass should be made. A history of diminution of libido or potency also is suggestive although these changes usually are so gradual that the patient may attach little significance to them. In the presence of positive physical findings or history, search for an adrenal tumor then should be made. Intravenous urography is comparatively easy to do and will demonstrate pressure changes in the position or outline of the calyceal pattern if the tumor is large. In 16 of the 17 patients in this series in whom an intravenous urogram was obtained a suprarenal tumor mass was demonstrated. The quality of contrast can be improved by retrograde dye injection. Retroperitoneal air insufflation is the best way to demonstrate small adrenal tumors, and, when combined with retrograde dye injection, will outline a very small adrenal mass. In certain patients aortography may be of value.

Laboratory studies may be of significance in the diagnosis of adrenal tumors in general. An increase in the urinary excretion level of the 17-ketosteroids has been a fairly constant finding in adrenal carcinoma, although normal levels have been found in some cases of carcinoma and are the rule in benign tumors. The number of cases of feminizing adrenal tumors is so small that only isolated studies of the 17-ketosteroids have been made. However, indications are that large quantities of 17-ketosteroids usually are excreted in the urine as demonstrated in the case here reported. Urinary estrogen and androgen studies may be helpful, but laboratory methods for routine clinical use of these studies are not available. A more detailed discussion of the laboratory features follows.

LABORATORY FEATURES

During recent years considerable light has been thrown upon the enormously complex subject of the adrenal corticosteroids and the effect on body function of these substances in health and disease. However, concepts are changing rapidly and the reader is referred elsewhere for a review of present concepts.[27] A detailed discussion of this subject is not within the scope of this paper; however, a brief review of the corticosteroids and the methods available for their study is appropriate.

Approximately 30 complex steroids have been isolated from the adrenal cortex and their chemical structures have been determined, and it is likely that additional hormonal substances will be found as studies continue. At the risk of over simplification, the physiologic effects of the adrenal cortex can be divided into three categories: (1) electrolyte and water metabolism, (2) carbohydrate, protein and fat metabolism and (3) control of sex characteristics.

Control over electrolyte and water metabolism is exerted chiefly by 11-desoxycorticosterone commonly used as the acetate and referred to as DOCA. This is a synthetic substance and recently aldosterone, formerly called electrocorten, has been isolated and found to have some 20 to 30 times the potency of desoxycorticosterone. This substance, or similar substances, through its effect on the renal tubules, the sweat glands, the salivary glands, the gastrointestinal

tract and the shift between the intracellular and extracellular compartments causes retention of sodium, chloride and water and increases the urinary excretion of potassium and phosphorus. Desoxycorticosterone also has a hypertensive effect, although this action is minimized when the adrenal cortices are intact. Measurement of the 24 hour excretion levels of desoxycorticosterone substances is not generally available. This phase of adrenal activity can be better studied by water and electrolyte determinations. The manifestations of adrenal insufficiency in Addison's Disease are largely correctable by the administration of this substance. In Addison's Disease there is also a diminution of other cortical activity as measured by a decrease in the urinary output of both the 17-ketosteroids and the glycogenic steroids. Consequently cortisone also may be useful in treating cases of Addison's Disease.

The second or cortisone phase of adrenal activity is concerned chiefly with carbohydrate and protein metabolism and probably to a lesser degree the metabolism of fat. Of the various compounds studied thus far, the most important and potent hormones in this group are 11-hydroxy-17-dehydrocorticosterone (cortisone or compound E of Kendall) and 17-hydroxycorticosterone (hydrocortisone). The important and far reaching effects of these substances both directly and indirectly through an interaction with other endocrine glands is becoming better understood, but their clinical usage in all types of disease states is not completely clarified. The manifestations of Cushing's syndrome are due largely to an excess of cortisone activity. The determination of the amount of urinary excretion of 17-hydroxycorticoids is an indicator of corticoid activity. Chemical determinations of the 11-oxyketosteroids also is a fair indication of the cortisone phase of adrenal activity.

Both androgenic and estrogenic compounds are produced by the adrenal cortex. Since the tendency toward virilism usually predominates in adrenal tumors or hyperplasia, this phase of adrenal activity sometimes is called the androgen effect. Cases such as that being here reported in which the feminizing effect predominates are rare. Cases of adrenal tumors in prepubertal girls with vaginal bleeding and sexual precocity probably represent the same dysfunction as cases of feminization in the male. Androgenic and estrogenic activity usually are measured by bio-assay methods which are far from satisfactory, although chemical measurements are now available. One would expect a direct correlation between the degree of masculinization and the quantity of urinary androgen, and between the intensity of feminization and the excretion of urinary estrogen, but this is not always the case in instances of adrenal tumors or hyperplasia. The ratio of one to the other as well as the quantity utilized by the body have been suggested as more important than the actual total urinary excretion.

Of the many measurements of adrenal activity, the one most commonly in use probably is the determination of the urinary 17-ketosteroids. This test measures the nonphenolic, neutral, 17-ketosteroids comprising in general most of the substances having androgenic activity, although certain androgens such as testosterone are not included, and other substances having no androgenic activity are included. Since these substances measured by 17-ketosteroid determina-

TABLE IV

Feminizing adrenal tumors

Hormonal studies

Case No.	Urinary Excretion per 24 Hours				
	Estrogens	Androgens	17-ketosteroids	11-oxysteroids	Gonadotropins
1	—	—	—	—	—
2	—	—	—	—	—
3	—	—	—	—	—
4	—	—	—	—	—
5	—	—	—	—	—
6	32100–6400 m.u./liter	60–100 c.c.u. /liter	—	—	A-Z test negative twice
7	—	—	—	—	—
8	—	—	—	—	—
9	—	—	—	—	—
10	4000–8000 m.u.	81 c.c.u.; 400–500 I.U.	—	—	Friedman-test negative twice 30–50 r.u./24 hrs
11	—	—	—	—	—
12	—	—	—	—	Friedman test positive pre-op & negative post-operation
13	5 r.u. no pregnandiol	—	4 mg.	—	F.S.H. assay negative
14	Equivalent pre-op to 5.3 mcg. of alpha-estradiol and postoperative to 9.5 mcg.	—	196–213 mg. pre-operative falling to 14.8 mg. post-op; beta fraction over 95% pre-op to normal rates post-operative	—	—
15	—	—	34 mg.; increased later to 108 mg.	—	—
16	—	—	23.2 mg.	—	—
17	250–500 I.U. of estrogenic hormone	—	6.0 mg.	—	Less than 20 m.u. excreted per 24 hours
18	—	—	7.6 mg.	—	A-Z test negative
19	5000 U./liter	—	6.9 mg.	—	48–96 U./liter of urine

20	Phenolsteroids .05 gamma; folliculin 275 gamma; estrogen 160 I.U.; pregnandiol 49.5 mg.	—	32–39 mg.	26 mg.	—
21	138 mcg. free oestriol/liter	—	—	—	—
22	—	1 r.u./liter	256 mg. increased later to 262 mg.	—	Friedman and frog tests negative
23	4000–8000 m.u. pre-operative 27–44 m.u. postoperative	—	12.4 mg. pre-op 7.8–14.9 post-op	—	24–48 m.u./24 hrs preoperative. Less than 8 m.u./24 hrs postoperative
24	460–660 m.u. 2 days postoperative decreasing later to 13–27 m.u.	—	5.8–6.9 mg.	—	24–48 m.u./24 hrs. postoperative
25	—	—	—	—	—
26	Average of 3341 I.U. post-op	—	29.3 mg. pre-op; 26.2–55.3 mg. post-op	—	A-Z test negative pre-op and post-operative
27	Estrone 86 gamma, estradiol 15 gamma, oestriol 57 gamma and pregnandiol 1.92 mg. pre-operative. Estrone 9 gamma, estradiol 10 gamma, oestriol 13 gamma and pregnandiol .034 mg. postoperative	—	30 mg. pre-op; 11.1 mg. post-op	—	—
28	Pregnandiol 621.6 mg.; estrogens 6.24 mg.	—	Levels up to 600 mg. with beta fraction as high as 71%	3.4 mg.	Quantitative Friedman test doubtfully positive F.S.H. titer 96 m.u.

tions are elaborated both by the adrenal and by the male gonads, levels in the male are somewhat higher than in the female. Likewise the levels show a progressive increase with age, showing highest levels around age 40 following which a gradual decrease occurs.

There are several different methods for determining the 17-ketosteroids, each showing slight differences in normal values with a fairly wide normal variation. The normal adult excretion in mg. per 24 hours is around 15 for males and 10 for females. The neutral 17-ketosteroids can be further separated into alpha and beta fractions by precipitation methods. The alpha fraction representing 85 to 90 per cent of the total probably is derived from both the adrenal and the male gonad while the beta fraction representing the remaining 10 to 15 per cent most likely consists of excretion products derived only from the adrenal cortex. In adrenal tumors there is an increase in the percentage of the beta fraction. It can, therefore, be seen that determination of the neutral 17-ketosteroids, while not a true index of adrenal androgenic activity, is sufficient for the purpose of most clinical work especially if the alpha and beta fraction are obtained. It must be remembered also that the liver plays a major role in the conversion of the adrenosteroids into 17-ketosteroids and such levels may be altered significantly in liver disease.

A summary of the laboratory findings in the reported cases is tabulated in table IV. Since many of these cases were studied before some of these determinations became generally available only spotty figures can be presented. A study of 24 hour urinary excretion of steroids was made in 16 of the patients in this review. The steroids studied were estrogens, androgens and 17-ketosteroids.

Estrogens: In all but 1 of the 12 patients in whom the urinary estrogens were studied there was an extremely large quantity excreted. Usually the quantity was as greater or greater than that found in a woman during pregnancy. In the 3 patients in whom the excretion of estrogens following removal of the adrenal tumor was compared to the pre-operative level of excretion a large reduction was found. Those patients in whom adrenal cortical carcinoma was found had the highest levels. The patients with adrenal cortical adenomas had lower levels and 1 was in the normal range.

Androgens: The urinary excretion of androgens was found to be increased in 2 of the 3 patients studied. In all 3 of the patients an adrenal cortical carcinoma was found.

17-ketosteroids: The urinary excretion of 17-ketosteroids was studied in 14 patients. In 4 patients there was a marked increase in excretion and adrenal cortical carcinoma was found in each patient. In 2 of these there was a marked increase in the beta fraction. In 6 patients there was no increase and only 1 of these was malignant. In the remaining 4 patients there was a moderate increase and in 2 of them an adrenal cortical carcinoma was found. In those patients in whom the excretion was studied following removal of the adrenal cortical tumor, a decrease in excretion was found. At times this was transient with a later increase as the carcinoma recurred.

11-oxysteroids: A study of these was made in 2 patients, and in 1 of them there

was an increased excretion. In this patient there also were other evidences of corticoid hyperfunction producing some of the features of a Cushing's syndrome.

Gonadotropins: The gonadotropins were studied in 12 patients. In 2 of them there was a very slight increase in the F.S.H. titer. In another patient there was a positive Friedman test pre-operatively which became negative after excision of an adrenal cortical tumor.

Carbohydrate Metabolism Studies: Alterations in glucose tolerance, insulin tolerance or the fasting blood sugar level were found in 3 patients. Two of these showed decreased glucose tolerance while the other showed hyperinsulinism.

Electrolyte Studies: These studies were fragmentary but were essentially normal in the cases in which they were done.

PATHOLOGIC FEATURES

Functioning lesions of the adrenal cortex have been studied frequently from the standpoint of their gross and microscopic morphology. Of the 28 patients, including our own, of feminizing lesions, 26 have been subject to pathologic examination. Of these, all lesions proved to be neoplasms with the coincidental occurrence of cortical hyperplasia in the patient of Luft and Sjögren.[12] In 19 patients the neoplasm proved to be malignant either histologically, clinically or both. One additional patient, that of Holl's case 1,[7] probably was a carcinoma although pathologic study was not made.

All malignant tumors except that of Staffieri, and associates[24] are recorded as carcinomas. This latter lesion is described as a sarcoma and seems to reflect almost complete reversion to the primordial mesenchymal celomic tissue from which the adrenal cortex is derived. Illustrations and descriptions of this tumor indicate focal differentiation into lipid laden cells resembling adrenocortical epithelium. No particular predilection toward laterality is apparent among the recorded cases. One instance of origin in an adrenocortical rest is suggested by Lisser.[11]

Of the remaining 8 cases, 6 almost certainly must be accepted as adenomas and probably benign. The second case recorded by Holl in all likelihood represented an unusually large and somewhat atypical adenoma. In the case of Cahill and associates[3] the diagnosis of adrenocortical tumor rests solely on clinical grounds.

The evidence would suggest a preponderance of malignancy in feminizing lesions of the adrenal cortex. The fact that 6 cases have been reported as adenomas should be accepted with the full knowledge that prediction of clinical behavior of adrenocortical tumors by histologic means is fraught with great difficulty unless frank invasion is demonstrable. Although encapsulation is a prominent feature of both benign and malignant tumors, the potential of such lesions to invade blood vessels is apparently in the magnitude of that experienced with hypernephroid carcinomas of the kidney. It would seem advisable, therefore, to institute prompt surgical investigation when feminizing adrenocortical neoplasia is suspected by the clinical studies outlined herein.

In general it may be stated that feminizing adrenocortical tumors tend to be round or ovoid and covered at least in part by a thickened capsule. They attain a size of several centimeters in diameter and may be palpable on abdominal

examination. In general the malignant varieties tend to be larger than the benign adenomas. The lesions are firm and sometimes fibrous on sectioning. Trabeculation of the cut surface has been a fairly constant feature producing a degree of lobularity comparable to hypernephroid carcinoma of the kidney. Their cut surfaces tend to be fleshy, reflecting a high degree of cellularity. They are frequently mottled red brown in color and highly vascular. Hemorrhage and necrosis is a prominent finding, particularly in the malignant variety, and cystic changes have been described several times.

The histologic morphology, although somewhat variable, usually has provided little difficulty in identification of adrenocortical origin. Cells of the three anatomic layers of the cortex may be found scattered about in disorderly arrangement in both benign and malignant varieties and both frequently contain spindle shaped or fusiform elements suggestive of dysembryoplasia. The lipid content likewise has been variable and mitotic activity may be found in profusion or may not be apparent. Invasion of the capsule and of the numerous endothelial sinusoids frequently has served as the only histologic criterion by which the malignant type could be differentiated from its benign counterpart.[8]

The identification of functional capacity by morphologic characteristics is thought at the present time to be impossible although certain inferences may well be practical as suggested below.

The pattern of metastases of malignant lesions has followed that of hypernephroid carcinomas of the kidney i.e. local invasion, venous invasion with spread to liver, lung and bone, and lymphatic extension to regional abdominal lymph nodes. A description of the pathologic aspects of the case which serves as the subject of this report will illustrate the salient pathologic features of this unusual neoplasm.

The fresh surgical specimen consisted of an ovoid tumor mass and the right kidney to which it was intimately adherent at the upper pole (fig. 4). The lesion was dissected free with the utmost difficulty due to invasion of the renal parenchyma extending almost into the compressed superior calyx. The tumor, which measured 9 by 9 by 7 cm. and weighed 321 Gm., was roughly lobulated in outline and partially encompassed by a thick fibrous capsule showing evidence of innumerable fibrous adhesions on its external surface. Large quantities of soft mottled hemorrhagic and yellow necrotic material extruded from an incision on its medial aspect. The tumor was sectioned with soft resistance disclosing variegated cut surfaces traversed by fibrous trabeculations. The parenchyma was composed of soft mucoid pink gray and brown tissue mottled by broad zones of hemorrhage and brilliant yellow necrosis. No blood vessels were observed grossly. No residual normal adrenal tissue was noted.

The histologic features of formalin and Zenker fixed sections were those of a malignant epithelial neoplasm displaying fairly accurate reproduction of adrenal cortical structure (fig. 5). Two cell types were found in the lesion. By far the more predominant were elements most closely resembling cells of the zona reticularis. These were somewhat variable in size and shape, some appearing fusiform or spindling, but the majority appearing rounded or polygonal. They

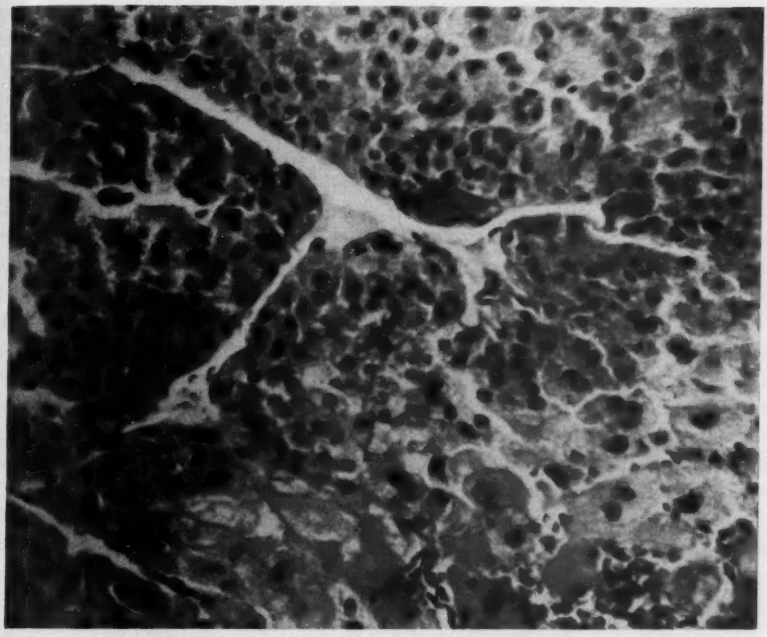

FIG. 5. Microscopic section of adrenal tumor × 300. Note two types of cells. The larger elements with homogeneous cytoplasm resemble zona fasciculata. The smaller more granular cells resemble zona reticularis. The rich capillary network is well shown.

contained an abundance of finely granular eosinophilic cytoplasm and small hyperchromatic nuclei generally in a central position. Prolonged search disclosed within them rare golden yellow brown pigment granules which stained positively for fat with Oil Red O, were acid fast, stained deep magenta with PAS and resembled greatly the lipofuscin or ceroid pigment often found in the zona reticularis of normal adrenals.

The second cell type was almost twice as large, more predominantly polygonal and contained large quantities of homogeneous clear or slightly foamy cytoplasm. Their nuclei were large, bizarre and strikingly hyperchromatic. Sections stained with Oil Red O and Nile blue sulphate disclosed a few scattered cytoplasmic lipid droplets of varying size. These were free of acid fast properties. These elements more closely resembled cells of the zona fasciculata although they lacked the characteristic corded arrangement.

The architecture throughout was exceedingly distorted. The cells were arranged in small clusters and occasional distorted cords. Numerous capillary and sinusoidal spaces lined with a single layer of endothelium rendered the tumor highly vascular and imparted an appearance quite typical of endocrine tissue. There was little supporting fibrous stroma except for the trabeculae that compartmentized the neoplasm. Extensive hemorrhage and necrosis were evident

within the growth. The ordinary difficulties of establishing benignancy or malignancy usually experienced with adrenal cortical neoplasms were obviated in this case by the ready demonstration of capsular and venous invasion. Mitotic activity, however, was not conspicuous.

Invasion of the upper pole of the kidney was confirmed histologically. Except for minimal chronic pyelonephritis, the renal findings were essentially normal.

As in the previously reported cases, attempts to determine the functional ability of the neoplastic tissue on a purely morphologic basis were fraught with disappointment. Only the preponderance of a cell type resembling the zona reticularis was helpful in suggesting that the tumor might elaborate hormones stimulatory to sex organs. Diligent search of sections stained by the method of Broster and Vines were fuitless for the demonstration of fuchsinophilic granules within the lesion. Fuchsinophilia once was considered a characteristic of virilizing adrenocortical lesions and it is of interest that in at least one previously reported feminizing tumor specific search for this feature likewise was negative. On the other hand similar cells have been described in normal adrenals of adult males and females, in cortical nodules, in at least one feminizing tumor and in nonfunctioning adenomas. In short, it has been generally concluded that fuchsinophilia or its absence bears little relationship to sexual function of the adrenal gland. As yet no method has been devised to demonstrate satisfactorily the presence of sex hormones in tissue by histochemical means so that this avenue of approach is not available.

Portions of tumor were submitted to the laboratory of Dr. Rosemary Schrepfer, Department of Obstetrics and Gynecology, Kansas University Medical Center for extraction and hormone assay. Estrogen was determined by means of the Kober color reaction and yielded 280 mg. from 70 Gm. of tumor tissue. The same sample yielded 4 mg. of pregnandiol as determined by the Guterman color reaction and 3.1 mg. of 17-ketosteroid as determined by the Zimmerman reaction. Although estrogen often has been demonstrated in the urine of patients with feminizing adrenal tumors, and its origin logically concluded as adrenocortical, this constitutes the first instance, to our knowledge, where such has been confirmed by chemical extraction of the lesion itself.

At autopsy the body showed a marked degree of wasting consistent with malignant neoplastic disease. The right breast was markedly enlarged in female contour and was composed of soft fleshy pearl white parenchyma containing no visible fat. The nipple was prominent and the areola deeply pigmented. The left breast was surgically absent. There was deep scleral icterus. The pubic hair was sparse and predominantly in female escutcheon.

A tumor mass measuring 18 by 12 by 8 cm. occupied the right renal bed extending downward from the diaphragm and infiltrating the adjacent soft tissues. This was mottled pink gray and brown and showed moderate lobularity on its anterior surface. The retroperitoneal, mesenteric and peripancreatic lymph nodes, as well as those of the portahepatis, were involved extensively by metastases. The vena cava in the region of the renal veins was enveloped by infiltrating tumor up to the level of the celiac axis. Its lumen was patent, however.

The liver, which weighed 5400 Gm., was replaced extensively by rounded

masses of tumor measuring up to 7 cm. in diameter. No biliary duct obstruction was demonstrated although the hepatic parenchyma appeared jaundiced.

Similar large round "*cannon ball*" metastases were scattered throughout both lungs which together weighed 1250 Gm. Except for passive congestion and edema, the lungs otherwise were normal.

An ovoid mass of metastatic tumor measuring 7 by 5 by 5 cm. had largely replaced the epiphysis and metaphysis of the right humerus at which site a pathologic fracture was evident.

The histologic features of the tumor were practically identical to that observed in the original growth. Broad areas of hemorrhage and necrosis were noted in many of the metastases while others appeared fairly well preserved. The effect of irradiation and nitrogen mustard therapy was impossible to assess.

Mitotic activity was perhaps somewhat more conspicuous in the metastases than the original tumor, but little or no lipid or pigment could be found and it was impossible to determine histologically the functional capacity of the lesion.

A 70 Gm. portion of metastatic tumor from the right humerus on extraction in Dr. Schrepfer's laboratory yielded 28.4 mg. of estrogen, 1.84 mg. of pregnanediol and 4.76 mg. of 17-ketosteroid. Thus the feminizing properties of the neoplasm were confirmed again by chemical means.

The secondary hormonal effects of the tumor were striking at autopsy. The breast, in addition to its feminine contour, showed histologic features consistent with prelactation (fig. 6). The ducts were dilated, showed evidence of proliferation and

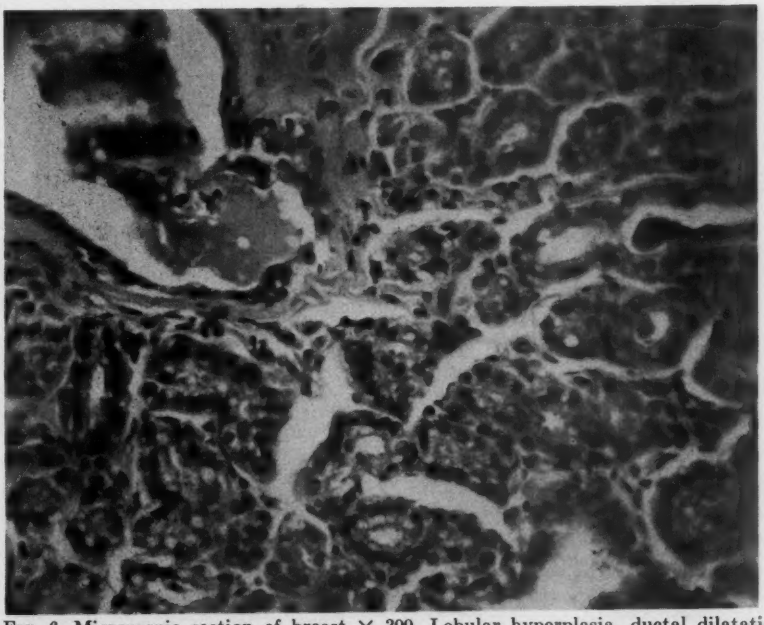

FIG. 6. Microscopic section of breast × 300. Lobular hyperplasia, ductal dilatation and secretory activity suggest prelactation state.

frequently were filled with secretion. There was profound lobule formation with hyperplasia. The lobular acini were lined with tall columnar cells containing prominent secretory vacuoles adjacent to the lumen. The hormonal mechanisms by which this remarkable hyperplasia was initiated is difficult to determine with certainty. Although estrogen alone might establish such a well integrated change in tubules and acini, one wonders if per chance the tumor may not have elaborated a lactogenic hormone or stimulated the pituitary to do so.

The testes likewise exhibited profound changes consistent with complete lack of pituitary stimulation. They were shrunken symmetrically to about one-half normal size. Spermatogenesis was totally deficient and no spermatogonia could be recognized (fig. 7). Sertoli cells were not significantly altered. A thick hyaline deposit was noted at the periphery of the tubules separating them from the tunica propria and representing alteration of the basement membrane. Interstitial cells could not be found. The prostate was not significantly altered.

Despite the findings within the testes, the hypophysis did not appear atrophic. It was slightly enlarged, measuring 15 by 12 by 7 mm., but the sella turcica was not widened nor was there erosion of the clinoid processes. The anterior lobe appeared faintly nodular. This was confirmed histologically by the finding of focal nodular multicellular hyperplasia. Eosinophiles were conspicuous throughout and, if there was any change, appeared increased. Basophiles appeared

FIG. 7. Section of testis × 120. Aspermatogenesis, absence of spermatogonia and hyalinization in the region of the tubular basement membranes are striking. Leydig cells scarcely can be found.

slightly reduced in number, frequently vacuolated and somewhat degranulated. No Crooke's cells or pregnancy cells could be found. The exact interpretation of these alterations is not possible.

The opposite adrenal gland was of normal size and position. Except for patchy depletion of cortical lipoid, no histologic alterations were seen. The thyroid was not remarkable. The parathyroid glands were not found.

The remainder of the examination failed to show evidence of other hormonal changes. Death appeared immediately related to infection originating within the left kidney which was the site of severe necrotizing pyelonephritis with total destruction of at least one papilla. Foci of degeneration with polymorphonuclear leukocytic infiltration within the liver and spleen suggested a terminal bacteremia or septicemia.

TREATMENT AND PROGNOSIS

As can be seen from a study of table III, the long term results following surgical removal of feminizing adrenal tumors have been poor. Of the 27 cases reported only 7 patients were alive at the time of the report, these patients having been followed for 6 months, 43 days, 4 years, 2 years, 5 months, 18 months, and 1 year. It is believed that these poor results can be attributed to the long period of delay prior to operation rather than to any property of high grade malignancy characteristic of this type of lesion. In fact there is considerable evidence to suggest that these tumors progress slowly and that surgical removal, if done in a reasonable period of time following the onset of symptoms, might result in a high rate of cure. There is little evidence of suppression of the pituitary or opposite adrenal in these patients so that no special precautions need be taken in the postoperative management as is necessary in other functioning adrenal tumors, although a severe drop in blood pressure occurred in one patient (case 25) when the tumor was mobilized and the operation had to be discontinued.

Since exposure of the opposite gland usually is unnecessary a lumbar approach with removal of the twelth rib, if necessary, is suitable in most patients although a combined thoracoabdominal incision may be necessary to obtain adequate exposure of large tumors. In either instance intraperitoneal exploration should be done for possible metastases.

These tumors, like all adrenal tumors, have not been materially benefited by roentgenologic treatment. Nitrogen mustard appeared to produce slight alleviation of pain in our patient, although this effect was temporary. The use of high dosage of androgen in an attempt to offset the estrogenic effects has been of little clinical value (case 18, 22).

SUMMARY

The production of feminizing changes by adrenal cortical neoplasms is rare. The clinical and laboratory features of the 27 such cases previously reported in medical literature are reviewed, and an additional case occurring in a 26 year old Negro is presented.

The most characteristic clinical features of these patients are gynecomastia, testicular atrophy, loss of libido, abdominal pain and a palpable tumor.

Laboratory studies on the reported cases have been sketchy; however, the only consistent finding has been an elevation of the urinary estrogen level, and study of the tumor by extraction and hormone assay in the patient of the case here presented has shown high estrogen levels in the tumor tissue.

Histologic study of these tumors shows a preponderance of cells resembling the zona reticularis; however, the general pattern in the feminizing neoplasm differs little from that found in other adrenal cortical tumors.

Follow-up studies on the reported cases indicate a poor prognosis, but improved diagnostic methods offer hope for improved results following surgical removal.

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PERSISTENT RIGHT BUNDLE BRANCH BLOCK DUE TO PULMONIC VALVOTOMY AND INFUNDIBULECTOMY*

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That various arrhythmias occur during cardiac operations is well recognized, accepted, and authenticated. Numerous electrocardiographic changes have been noted and variously attributed to hypoxia, vagal reflexes, blood pressure changes, altered dynamics of the cardiovascular system during operation, and direct mechanical stimulation of the heart. Generally these changes are transient and of no permanent significance although in a few instances ventricular fibrillation may occur.[3-6]

Most recently the electrocardiographic findings during pulmonic valvotomy in 70 cases have been discussed in detail.[2] Changes in the pacemaker, nodal rhythms, and atrioventricular dissociation were noted and believed due to the anesthesia. Ventricular extrasystoles and bursts of ventricular tachycardia were frequent. The latter were noted during injection of procaine into the myocardium and during the valvotomy or infundibular resection. Bundle branch block is mentioned as a temporary occurrence.

We can find no reference to bundle branch block being precipitated by pulmonic valvotomy or infundibulectomy with its persistence postoperatively. This feature has been noted in 4 of our 31 patients undergoing a Brock procedure, 17 for tetralogy of Fallot and 14 for isolated pulmonic stenosis.

CASE REPORTS

Case 1. Tetralogy of Fallot. C. C., an 8 year old girl was asymptomatic until 1 year of age when she developed left hemiplegia. Subsequently she has had persistent cyanosis (peripheral oxygen saturation, 70 per cent preoperatively). Electrocardiogram before operation showed right ventricular hypertrophy.

A Brock type infundibulectomy was done on Sept. 4, 1954. The child obtained marked relief of cyanosis (peripheral arterial oxygen saturation, 96 per cent postoperatively). Numerous electrocardiograms taken postoperatively have shown right bundle branch block (fig. 1).

Case 2. Tetralogy of Fallot. L. S. was a 22 year old man with cyanosis since the age of 10 months. Subsequently he developed increasing dyspnea and decreasing exercise tolerance. A Brock procedure was done on Jan. 19, 1953 with incision only of infundibular stenosis. Temporary improvement of symptoms and signs resulted, but six months later cyanosis had returned with decreased exercise tolerence.

A second Brock procedure was done on June 16, 1954 with infundibular resection. Postoperatively cyanosis disappeared and exercise tolerance improved markedly (peripheral arterial oxygen 64 per cent saturation preoperatively, 87 per cent postoperatively). All electrocardiograms before the second operation had shown only right ventricular hyper-

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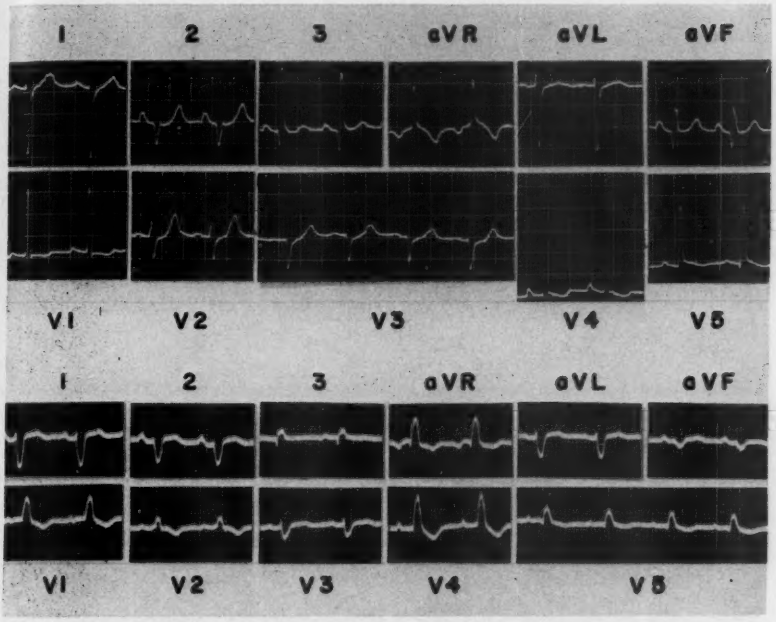

FIG. 1. C. C., tetralogy of Fallot. The electrocardiogram above was taken preoperatively, the one below one week following a Brock type infundibulectomy. Preoperatively the electrocardiogram shows right ventricular hypertrophy with a QRS interval of 0.05 seconds in lead 2. Postoperatively there is a right bundle branch block with a QRS interval of 0.11 seconds in lead 2. Note the slurring of QRS complexes in all leads.

trophy. Right bundle branch block was noted during the operative procedure in 1954 (fig. 2) with persistence in all electrocardiograms taken subsequently (fig. 3).

Case 3. Isolated valvular pulmonic stenosis. A. N. was a 13 year old girl who was asymptomatic until age 11 years. At that age she noted exertional fatigue, palpitations, and exertional dyspnea which have persisted until operation. Pulmonic valvotomy was done on Aug. 3, 1954. Postoperatively she has been completely asymptomatic.

Preoperative electrocardiograms showed only right ventricular hypertrophy. Several electrocardiograms made postoperatively have shown right bundle branch block (fig. 4).

Case. 4. Tetralogy of Fallot. L. D. was a 17 year old boy who had had cyanosis and exertional dyspnea since birth. No history of squatting could be obtained. At age 6 years he had an attack of subacute bacterial endocarditis. In addition this boy also had congenital vesicle neck contracture with hydroureter, hydronephrosis, and persistent azotemia.

On April 23, 1953 a Brock procedure was done with multiple incisions of a pulmonic valvular stenosis. Subsequently he has had much improvement in exercise tolerance and decrease in his cyanosis.

Preoperatively electrocardiograms were within normal limits, but postoperatively numerous electrocardiograms have shown right bundle branch block (fig. 5).

OPERATIVE TECHNIC

Our technic for pulmonic valvotomy or infundibulectomy is essentially that described by Brock with a few modifications.[1] The patient is placed in a supine

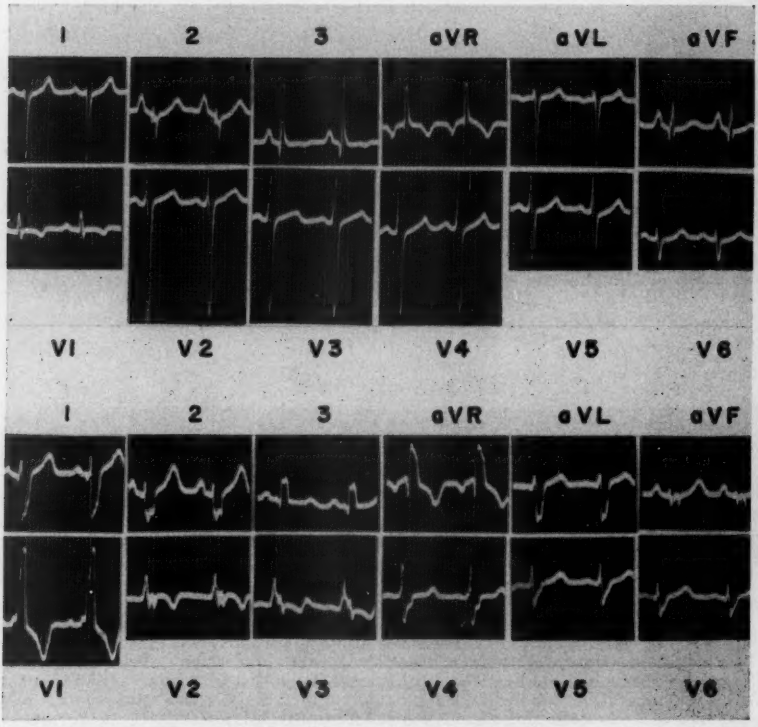

FIG. 2. L. S., tetralogy of Fallot. The electrocardiogram above was taken prior to the second Brock procedure and the one below 14 days postoperatively. Preoperative tracing shows right ventricular hypertrophy with a QRS interval of 0.08 seconds in lead 2. Postoperative tracing shows right bundle branch block with QRS duration of 0.12 seconds in lead 2 and slurred, notched QRS complexes in all leads.

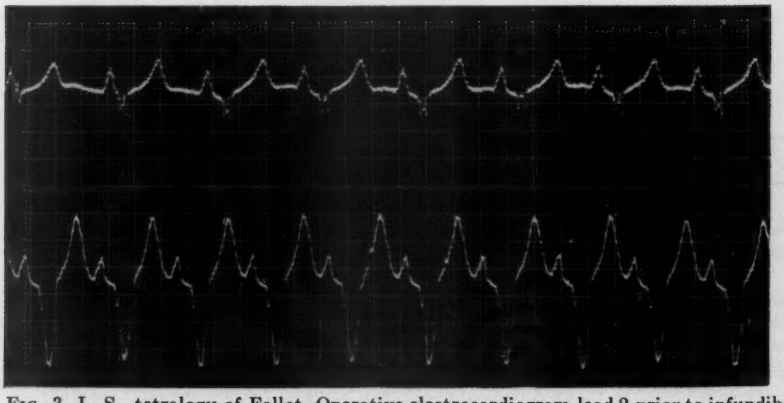

FIG. 3. L. S., tetralogy of Fallot. Operative electrocardiogram lead 2 prior to infundibulectomy and immediately after initial resection of infundibular area. The QRS duration has changed from 0.08 seconds to 0.14 seconds. Note the sinus rhythm in both strips with an increase in rate from 84 to 108 per minute.

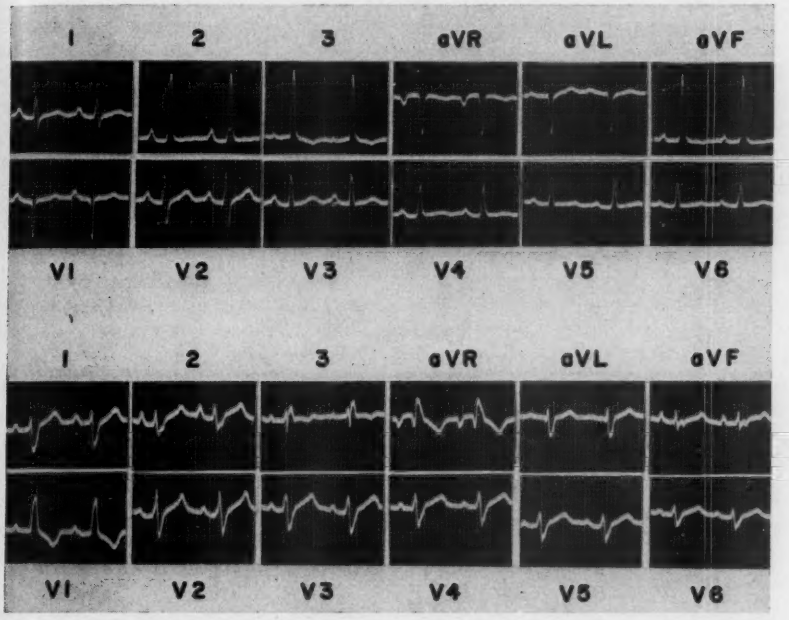

FIG. 4. A. N., isolated valvular pulmonic stenosis. The tracing above was taken preoperatively and the one below postoperatively. The typical pattern of right ventricular hypertrophy is shown preoperatively with the QRS complex being 0.07 seconds in lead 2. Postoperatively the QRS has increased 0.12 seconds with slurring and notching of this complex.

position with the left shoulder slightly elevated. Electrocardiograpic leads are attached for tracings as desired. Utilizing an inframammary incision the pleural cavity is entered through either the fourth or fifth interspace. The costal cartilage of the fourth or fifth rib is transected parasternally to afford further exposure if necessary. The lung is collapsed posteriorly and the pericardium is incised parallel and anterior to the phrenic nerve. After inspection and palpation of the heart and great vessels, pressure tracings are taken in the aorta, right ventricle, and pulmonary artery.

A purse-string suture is placed in the midportion of the right ventricle in its relatively avascular portion. At present we do not inject procaine into the myocardium since in earlier cases we were unable to appreciate any difference in those in whom it was employed and those in whom it was not used. A stab wound is made into the area circumscribed by the suture and the stenosis, if valvular, is incised with either the Brock or the Potts valvulotome. If an infundibular stenosis exists, this is first explored with the Brock valvulotome and then resected with a Brock infundibulotome of the appropriate size. Pressure tracings are repeated after an adequate opening seems present. The incision in the right ventricle is closed by tying the purse-string suture, and employing an additional mattress

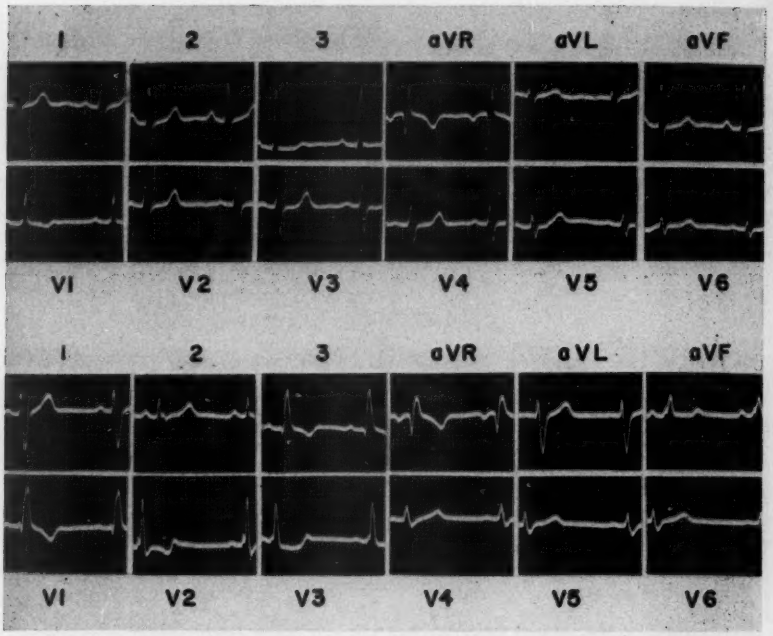

FIG. 5. L. D., tetralogy of Fallot. The tracing above was taken preoperatively and the one below postoperatively. Preoperatively the electrocardiogram shows right ventricular hypertrophy with a QRS of 0.08 seconds in lead 2. Postoperatively the QRS duration has increased to 0.12 seconds, right bundle branch block being present.

stitch when necessary. The pericardium then is loosely approximated with interrupted silk sutures.

DISCUSSION

Right bundle branch block may be found in people with an otherwise entirely normal cardiovascular system. Its presence in congenital heart disease usually is associated with and considered indicative of right ventricular hypertrophy and hypertension. It is more frequently found in instances of isolated pulmonic stenosis than in tetralogy of Fallot. In the evolution of right ventricular hypertension there often is the gradual change from a pattern of right ventricular hypertrophy to one of right bundle branch block.

In the cases presented here no evidence of right bundle branch block was noted preoperatively. However, the electrocardiogram taken during operation or soon thereafter showed right bundle branch block which has persisted as long as these patients have been observed. The patient in case 4 is slightly more than two years postoperative.

It is interesting to speculate as to why such a change has developed when the obstructing lesion has been excised or incised with subsequent relief of symptoms and concomitant lowering of the right ventricular pressure. The most ready explanation is that operative trauma has damaged conduction fibers in the inter-

ventricular septum either directly or indirectly by edema, ischemia, and fibrosis sufficient to cause permanent changes in conduction. Since most of the conduction bundle branches lie in the posterior portion of the interventricular septum, this explanation may not be valid. Recently, however, in the creation of interventricular septal defects experimentally in dogs by punching out a core of tissue, right branch block was encountered in 20 of 25 animals.[7]

It does not seem probable that either placement of the purse-string suture or the right ventriculotomy is cause enough for this electrocardiographic abnormality since this trauma is confined to the anterior wall of the right ventricle. Although we did not inject the area of cardiotomy with procaine, as was described by Brock, it would appear unlikely that this maneuver is of sufficient significance to explain the occurrence of right bundle branch block.

The right ventricular pressures in these patients varied from 70 to 175 mm. of mercury preoperatively. That each patient was on the verge of developing right bundle branch block at the time of the operation, and that sufficient additional strain was placed on the right ventricle by the cardiotomy to cause right bundle branch block, hardly seems probable. If this were true one might expect disappearance of the right bundle branch block several weeks or months after operation when the right ventricle had healed and had adjusted to its decreased work load.

These patients have had no deleterious symptoms nor has their clinical course varied in any way to correlate with the finding of right bundle branch block. It is suggested that right bundle branch block may be a common finding after the Brock procedure.

SUMMARY

The incidental finding of persistent right bundle branch block in 4 of 31 direct operations for pulmonic stenosis is presented. Three of these patients had tetralogy of Fallot, 2 with infundibular and 1 with valvular stenosis. The other patient had isolated pulmonic valvular stenosis.

Operative trauma to conduction bundle branches in the interventricular septum is suggested as the etiology.

The occurrence of this conduction abnormality had no appreciable significance on the clinical course of these patients or their operative results.

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KRUKENBERG TUMORS

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Krukenberg tumors are an intriguing pathologic and clinical entity. They are interesting because they represent a peculiar predilection for secondary ovarian growth which cancer of the stomach and less often other gastrointestinal malignancy or breast carcinoma may manifest. Often this metastasis occurs without signs of spread elsewhere and with the mode of spread from the stomach to the ovary obscure.

HISTORIC BACKGROUND

Interestingly, the man for whom the tumor was named and whose description of the tumor is classical, Friedrich Krukenberg,[10] failed to recognize either the secondary nature of the disease or its epithelial origin. He called it "fibrosarcoma ovarii mucocellulare carcinomatoides" and described 5 cases in 1896. In 1902 three other German workers,[7] Schlagenhaufer[18] followed by Wagner[19] and Romer,[17] pointed out the metastatic nature of the tumor as well as its epithelial origin. Today, the term "Krukenberg tumor" implies a secondary carcinoma of the ovary. Although a few apparently primary Krukenberg tumors have been reported, they generally are viewed with some skepticism. Lowman,[13] Ackerman,[1] and Leffel and associates[11] believe that the term "Krukenberg" should be discontinued and that a "metastatic ovarian tumor" should be designated simply as such.

INCIDENCE

In reviewing the literature one gathers that Krukenberg tumors are fairly rare. Leffel and co-authors described 44 cases seen at the Mayo Clinic in the 30 years between 1908 and 1938. Costello,[4] in 1947, stated that there were less than 200 cases recorded in the literature at that time. Andrews,[2] in 1954, stated that probably not more than 300 cases of Krukenberg tumor had been reported.

PATHOLOGY

Although Krukenberg failed to recognize that this was a secondary tumor of epithelial origin, nevertheless, his careful description of this lesion has not been improved upon and renders its identification unmistakable. He stated that the tumor usually is bilateral and usually occurs in young women. It is slow-growing and often associated with ascites. There usually is enlargement of the whole ovary and the form of the ovary is preserved even though the surface may be nodular. On the cut surface the consistency is usually hard, but cysts may be present in the myxomatous tissue. Microscopically there are round, swollen cells with mucinous protoplasm which frequently have the characteristics of epithelial cells. The tissue has an eczematous character and apparently repre-

sents a mucinous metamorphosis of the cells. The nucleus, located in the periphery of the cells, has a signet ring form.

Jarcho[8,9] stated that all ovarian tumors which enlarge the ovary uniformly without distortion and which present alternation of fibrous areas and mucinous cell groups, and which propagate along the lymphatics, should be called Krukenberg tumors. It also is his belief that signet ring cells are not necessary for this diagnosis.

The mode of spread of this tumor is through four possible avenues: 1) lymphatic, 2) blood stream, 3) direct continuity, and 4) seeding from the peritoneal fluid. Although all four modes of metastasis can and no doubt have on occasion occurred, it seems likely that the lymphatic spread is the most plausible in most instances.

Amann[2] in 1905 thought that retrograde lymphatic spread to the ovarian lymphatics occurred when the retrogastric and superior lumbar lymph nodes were invaded. This would be consistent with the type of growth that occurs in the ovary which maintains the ovarian shape as though the tumor invaded by way of the medulla rather than the surface. Novak and Gray,[16] in their report of 21 cases, believed that lymphatic spread is the most frequent. Major, in 1918,[14] reported a case of Krukenberg ovarian tumor secondary to gastric carcinoma, in which typical signet ring cells were found on microscopic examination in the blood vessels of the lungs. This indicates that hematogenous spread occasionally occurs.

CLINICAL COURSE AND TREATMENT

Krukenberg tumors usually are associated with a rapidly fatal outcome. In the cases reviewed by Leffel and associates at the Mayo Clinic between 1908 and 1938, the average length of life after removal of a Krukenberg tumor was found to be 3.61 months and the longest life 12.8 months in the case of a Krukenberg tumor primary in the sigmoid colon. McDuff[15] reported a case in which the patient was living 17 months after oophorectomy for Krukenberg tumor secondary to carcinoma of the breast removed six years before.

The average age incidence of patients who have this disease seems to be about 35 years according to most authors, although the patients in the cases of Leffel and co-authors had an average age of 48.2 years. They reported a Krukenberg tumor in a patient 13 years old arising from a carcinoma of the sigmoid, who died three months after the first symptoms.

Although the overwhelming majority of these cases are secondary, there is evidence of a primary origin occasionally. Novak and Gray reported 2 cases without evidence of carcinoma in the gastrointestinal tract or without evidence of recurrence, one 4 years and one 3¼ years postoperative. Andrews[3] reported the case of a patient living 13 years after the removal of a Krukenberg tumor in whom no primary lesion was ever found.

In the cases of Leffel and associates, ascites was present in 17 patients and absent in 27. The lesion was bilateral in 35 patients and unilateral in 9. In 30 patients a primary lesion was diagnosed first. The primary lesion was unknown

in 3 patients. In 20 patients the stomach was the source of origin, the large bowel in 13, the uterus in 1, the breast in 1, and the small bowel in 2 patients. They concluded that surgery is not indicated in extensive metastases or poor surgical risk, but in a good risk the uterus, tubes and ovaries should be removed, because, first, the pathologic diagnosis may be wrong, second, the patient's life is made more comfortable, and third, the increase in mortality and morbidity is small from the operative procedure. The uterus may occasionally be left but one ovary should never be left. Surgery may be more radical when the primary lesion is in the colon for these are often low grade malignancies.

Jarcho[9] stated that the blood and lymphatic supply and hormonal influences cause greater growth of carcinoma in the ovaries than elsewhere, although there is a carcinomatous lymphangitis present. Therefore, since radical extirpation of the uterus and tubes will in no way affect the microscopic metastases elsewhere, he concludes that it is not justified. Costello quotes Falkner and Douglas as offering the hypothesis that these huge ovarian tumors represent some kind of defense reaction against the inroads of the primary growth with the patient maintaining her weight with minimal symptoms until discovery and removal of the ovarian tumors, after which she goes rapidly downhill.

Some unusual cases of Krukenberg tumors have been reported. Zeigerman,[20] in 1948, described a case in which osteoblastic bone metastases occurred, although most cases showing bone metastases are osteoclastic. London and Grossman,[12] in 1949, recorded a case of Krukenberg tumor of the testis from a primary carcinoma of the stomach in a 38 year old man, who died 4 months after the orchiectomy. Dick and associates,[5] in 1950, reported a case of Meig's syndrome with Krukenberg tumor primary in the stomach. Ellman[6] had a patient with a Krukenberg tumor of the ovary, presenting a pleural effusion and resembling a Meig's syndrome.

CASE REPORT

This patient, a 38 year old Negro woman, was admitted to the hospital on March 6, 1951. She had had vague stomach complaints for a little over four months and vomiting for several weeks prior to admission. A gastrointestinal roentgenologic series showed a partially obstructing pyloric lesion. On admission she was rather emaciated and anemic, weighing 94 lbs., and had a hemoglobin of 58 per cent. On March 8, a gastric resection was done. There was a hard lesion at the pylorus about 6 cm. in diameter which was adherent to the pancreas. There were much enlarged lymph nodes extending from the celiac axis to the superior mesenteric artery, along the aorta. The liver was uninvolved. Convalescence was uneventful but the operation was considered only a palliative one.

Pathology Report: Gross examination of the surgical specimen consists of a portion of the stomach measuring approximately 18 cm. along the greater curvature. Near the pyloric end of the specimen there is an indistinct indurated area measuring 3 by 2.5 cm. with localized thickening of the wall and apparent superficial ulceration of the mucosa. Near this area there is a deep hunched-out ulcer measuring 3 by 2 cm. with a depth of 1 cm. Gross section shows fibrous thickening of the ulcer base which apparently penetrates completely through the muscular coat. The submucosa at the ulcer edge also shows extensive thickening. Five small firm lymph nodes, the largest of which measures 8 cm. in diameter, are located in the mesentery attached opposite the area of ulceration.

Microscopic section through the ulcer shows a floor composed of characteristic granula-

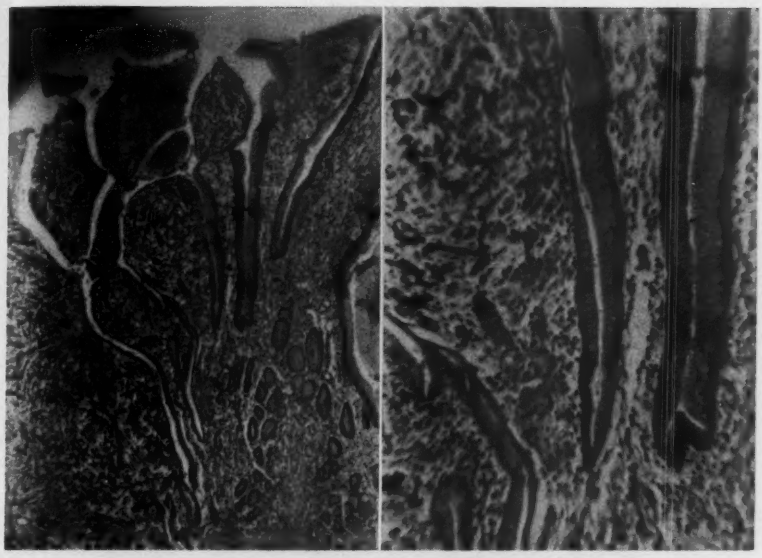

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FIG. 1. Photomicrographs showing the edge of the malignant ulcer of the stomach. (a) Low power; (b) High power.

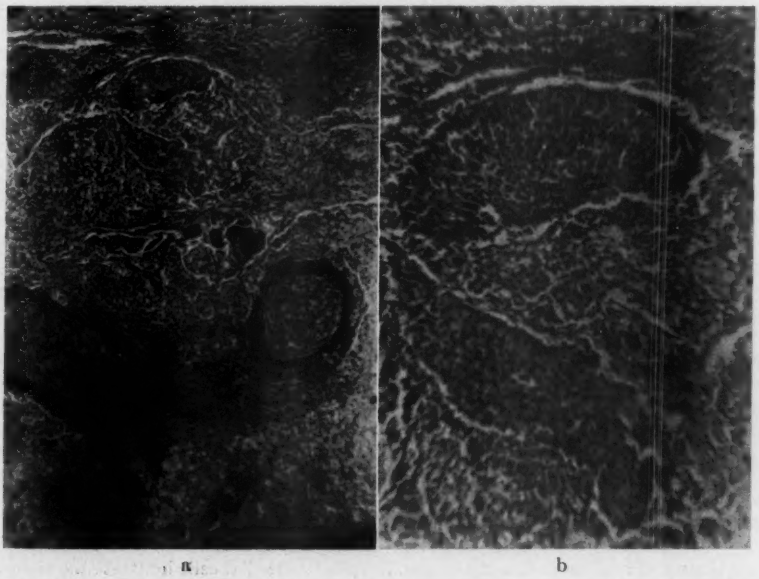

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FIG. 2. Photomicrographs showing lymph node metastasis of the stomach carcinoma. (a) Low power; (b) High power.

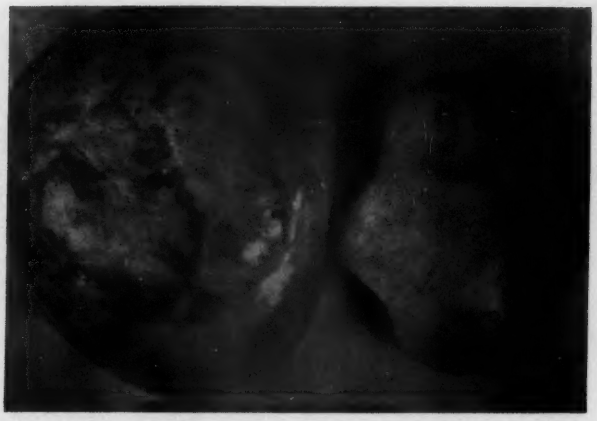


FIG. 3. Photograph showing the ovarian tumors relative sizes of which are indicated by the 6 inch ruler at the bottom of the picture.

tion tissue. The crater extends through the entire thickness of the muscularis into the adjacent thickened and fibrotic serosal layer. Neutrophils are near the surface. The adjacent submucosa at the ulcer border shows extensive fibroblastic proliferation, edema, inflammatory cell exudate, and also innumerable small nests and cords of atypical epithelial cells with moderately rounded chromatic nuclei and a moderate amount of pinkish cytoplasm. Transformation of the glandular epithelium into nests and strands of atypical cells is not a conspicuous feature and requires search for demonstration. A tendency toward small acinar formation can be made out in a few places. An occasional tumor cell also demonstrates a vacuole and in rare instances a slightly flattened nucleus occupies a peripheral position. The neoplastic cells infiltrate extensively beneath the ulcer base and extend into the serosa. The lymph nodes all show reactive hyperplasia of varying degree and two of them contain metastatic tumor. The large metastasis demonstrates extensive transformation of the atypical epithelium and the large cells have a slightly granular or clear vacuole with compression of the nucleus to one side.

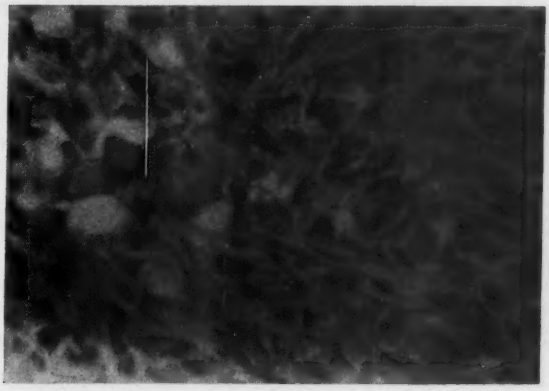
Diagnosis: Malignant gastric ulcer with lymph node metastasis. Figures 1 and 2 show photomicrographs of the lesion.

The patient was seen again early in May of 1952, one year after the gastric resection, complaining of a progressively enlarging lower abdominal mass of six months' duration. She had had menstrual periods every three weeks, but the large mass extending above the umbilicus was suggestive of a six or seven months' pregnancy. A Friedman test was negative. A tentative diagnosis of a Krukenberg ovarian tumor was made. Laparotomy was done on May 13, and two massive ovarian tumors were removed. There were no other evidences of metastatic deposits in the peritoneal cavity and the liver was free of metastases. The aortic nodes which had been noted to be enlarged at the time of the gastric resection showed no change. She made an uneventful convalescence after this operation.

Pathology Report: Gross examination of material submitted shows two irregular segments of grayish white tissue each of which measures approximately 12 cm. in greatest diameter. The cut surface shows innumerable small cysts averaging 1.5 cm. in diameter with a number of pale, irregular fleck-like areas (Fig. 3).

Microscopic sections show rather diffuse fibrosis throughout the ovaries with numerous small masses of neoplastic-like structures. Atypical epithelial cells infiltrate the tissue. In some areas there is a tendency toward acinar formation and rather well vacuolated cells are present. In other areas the cells are small and deeply stained. Comparison of sections

a



b

FIG. 4. Photomicrographs of the ovarian tumor. (a) Low power; (b) High power

made from the tumor found in the ovary with those of the stomach which was removed surgically at an earlier operation shows the same cell type.

Diagnosis: Krukenberg tumor of the ovary. Figures 4 and 5 show the photomicrographs of the ovaries.

Follow-up of the patient's course following the removal of the Krukenberg tumors showed the patient to be completely asymptomatic and without evidence of recurrence on the last of July 1955, over four years from the time the stomach was removed and over three years from the time the Krukenberg tumors were removed. This is a longer survival time following removal of a Krukenberg tumor, secondary to carcinoma of the stomach, than we have been able to find in the literature.

SUMMARY

Krukenberg tumors are an interesting secondary carcinoma of the ovaries which usually are primary in the stomach or elsewhere in the gastrointestinal tract. It is a fairly rare disease with only 300 cases said to have been reported

up to 1954. A few primary Krukenberg tumors of the ovary have been described but these are so rare that a primary disease elsewhere must always be postulated and searched for whenever a Krukenberg tumor is diagnosed.

The clinical course of a patient following the removal of Krukenberg tumors usually is a rapidly fatal one, the average length of life being considerably less than six months. When the primary lesion is in the stomach, the retrogastric lymph nodes are thought to be universally involved prior to the development of the tumor in the ovary. Therefore, it would seem that only simple removal of the ovaries for a Krukenberg tumor would be as effective as the more radical panhysterectomy, since the lesion is obviously incurable in any event. This premise seems to be borne out by the case report given here since this patient had only a simple removal of the ovaries and has lived without evidence of recurrence for over three years following this procedure, which is longer than any similar case reported in the literature. Apparently the length of life following the diagnosis of a Krukenberg tumor depends more on the grade of malignancy than on the operative procedure. Leffel and associates[11] emphasized that Krukenberg tumors, secondary to colon carcinoma, often are of a much lower grade malignancy than those from the stomach.

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FATAL REBLEEDING INDICES IN DOGS FOLLOWING ADMINISTRATION OF BLOOD, PLASMA, DEXTRAN, AND CRYSTALLOID SOLUTIONS*

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INTRODUCTION

Many laboratories, including our own, have contributed convincing evidence that dextran and several of the other high molecular weight solutions are highly efficient in immediate re-expansion of an acutely depleted blood volume. This expansion is manifest in the plasma volume and partially at the expense of hemodilution of the remaining red cell mass. It was the purpose of this study to approach the problem of restoration of blood volume in a somewhat different manner, viz. to assay the vulnerability of dogs treated with the repair solutions and then subjected to a second hemorrhagic insult by fatal rebleeding.

METHODS

Mongrel dogs weighing between 10 to 18 kilograms were chosen as the experimental animals. They were anesthetized lightly with intravenous pentobarbital and the left femoral artery and vein were surgically exposed. A standardized, rapid, bleeding was done from the femoral artery to a volume calculated on the basis of 4 per cent of body weight. In general, this percentage decreases the blood volume of the animal approximately 50 per cent. Immediately after bleeding, an infusion, the exact volume of which equalled the blood withdrawn, was administered briskly into the femoral vein. This required 3 to 5 minutes for completion.

The infusions consisted of the following repair solutions: donor's own blood, plasma, dextran, 5 per cent glucose in physiologic sodium chloride solution, and physiologic sodium chloride solution. Each series consisted of 10 animals, including a control group which received no replacement therapy whatsoever. Initial blood volumes (IBV) were determined on each animal, and at 1 hour and 24 hours after bleeding. At 24 hours, the animals were subjected to a fatal rebleeding procedure from the opposite (right) femoral artery. Fifty cubic centimeters of blood were withdrawn every 4 minutes until the animal died and the total fatal rebleeding volume was recorded (FRV). These fatal rebleeding volumes were compared with the initial blood volumes to arrive at the fatal re-

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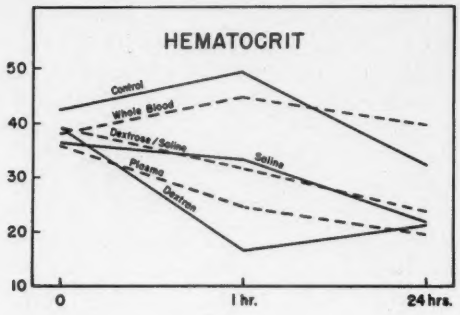

FIG. 1

bleeding index (FRI or FRV/IBV). Blood volumes were determined by T-1824 with a precision error of 1.62 per cent.

RESULTS

The hematocrit, plasma volume, and blood volume data are graphically presented (Figs. 1, 2, 3), and will be discussed briefly inasmuch as they document the course of events during the first 24 hours after initial bleeding, just prior to the FRV determinations.

Dextran: There is a marked rise in the plasma volume and a lesser concurrent increase in the blood volume. Actually, there is over-expansion of the plasma volume. It would seem that, initially, the majority of the macromolecular dextran is retained in the blood vascular compartment. The falling hematocrit reflects the hemodilution effect. At 24 hours, the plasma and blood volume levels decline while the hematocrit increases. This suggests that dextran is beginning to be lost from the vascular bed.

Blood: At one hour, the blood volume actually is increased along with the hematocrit. This is most likely due to splenic contribution of red cells.

Plasma: At 1 hour, the plasma volume increases while the over-all blood volume decreases somewhat. The drop in hematocrit is consistent with a loss

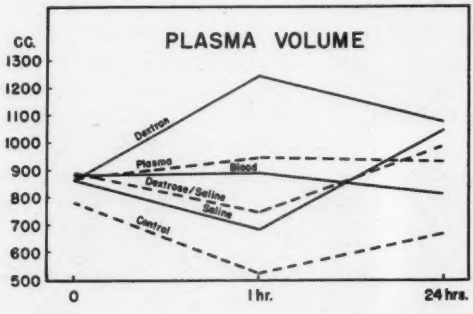

FIG. 2

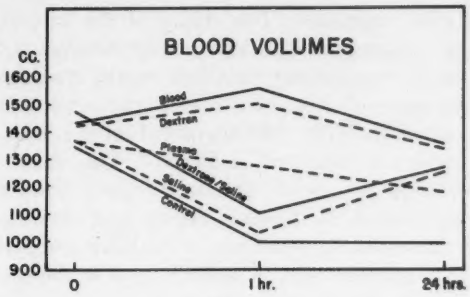

FIG. 3

of red cell mass by hemorrhage plus the hemodilution effect of plasma administration. Plasma and blood volumes both decrease within 24 hours indicating some plasma loss into the extravascular space.

Crystalloids: The response to 5 per cent glucose in physiologic saline and physiologic saline solutions will be considered jointly. The plasma and blood volumes, and also hematocrit, all fall sharply in 1 hour. This is attributed to, (1) loss of whole blood by hemorrhage, and (2) the rapid movement of the crystalloid repair solutions out of the blood vascular space. Within 24 hours, there is an increase in plasma and blood volumes with an associated falling hematocrit suggesting remobilization of extravascular fluid back into the blood stream. The effect is a "delayed restoration of blood volume."

Controls: Initially there is a significant drop in plasma and blood volumes as would be expected following untreated hemorrhage. Within 24 hours, the lowered hematocrit and partial recovery of plasma volume probably are on the basis of compensatory autoinfusion.

The foregoing data are not startling; in fact, they are consistent with our current concepts of hemodynamics of circulation and physiologic principles of the crystalloid and macromolecular solutions. The results observed with the fatal rebleeding indices (FRI) are considered to reflect an accurate picture under

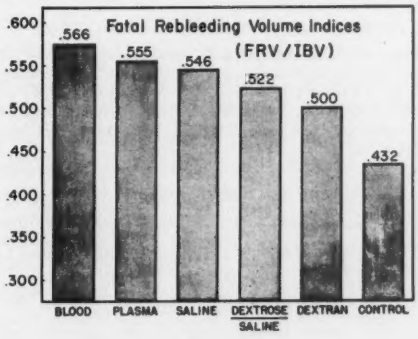

FIG. 4

the conditions of this experiment. The ability of the subject to withstand a second hemorrhagic onslaught should be a useful measure of the adequacy of the earlier therapeutic replacement; in other words, the higher the index of fatal rebleeding, the more efficacious has been the attempt with repair solutions at blood volume restoration. The FRI computed on the basis of a mean of 10 animals in each series are presented in figure 4. This data was subjected to statistical analysis by Chi-Square (X) testing and the differences in these indices are of statistical significance. It therefore can be said that blood is superior to plasma; plasma is superior to crystalloids; crystalloids are superior to dextran; dextran is superior to no treatment as demonstrated in the controls.

DISCUSSION

Dextran actually over-expands the plasma volume and in this respect is superior to the other repair solutions employed. Such mechanical expansion with a relatively inert macromolecular solution may not necessarily be beneficial. McCarthy and associates have demonstrated that physiologic sodium chloride solutions are superior to macromolecular solutions in promoting 10 day survival in experimental burns.[2] In hypovolemic shock, isotonic saline administered in a quantity to approximate the volume distribution, i.e. approximately two and one-half times volume of blood lost, maintained blood volume as well as did dextran.[1] The majority of administered crystalloid solution is lost almost immediately into the extra-vascular compartment. Subsequent remobilization and autoinfusion of this now "plasma like" fluid results in a delayed, albeit more physiologic blood volume restoration. The results of the fatal rebleeding indices would seem to support this concept.

SUMMARY

Dextran is superior to other repair solutions in its immediate plasma volume expansion 1 hour after hemorrhage.

The fatal rebleeding index (FRI) of dextran 24 hours after initial hemorrhage and therapy, is inferior to indices of other repair solutions used. It affords the least protection against a fatal rebleeding of the experimental animal.

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LONGITUDINAL GROWTH OF LOWER EXTREMITY FOLLOWING EXPERIMENTAL PARTIAL PERIPHERAL DENERVATION*

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The clinical observation that longitudinal bone growth impairment occurs in paralysis resulting from poliomyelitis has led many to inquire into its cause.[2, 4] Stinchfield, Barr, and Reidy[6] have reported that the resulting growth discrepancies can be predicted by estimation of the extent of paralysis in the affected limb. From this report it might be inferred that the length growth disturbance is directly proportional to the extent of paralysis. This has not been our clinical experience, since totally paralyzed extremities of some patients occasionally appear to grow almost normally while in other patients a relatively minor degree of weakness will be associated with a significant degree of shortening.

The role of the sympathetic nervous system in the growth disturbance following poliomyelitis is at present unknown. Sympathectomies sometimes will result in an increase in growth of an extremity in the human being, but animal experimentation has consistently failed to duplicate this finding.[1] Howell has shown that following peripheral denervation in dogs, if the animal is kept off weight bearing, a significant degree of length growth discrepancy is noted after nine weeks.[3]

EXPERIMENTS

The purpose of these experiments was to determine whether significant disturbance in the growth of bone in length would result from peripheral denervation alone, if the animals were allowed normal activity during the growth period.

Young male goats were selected for the experimental animals because they are not subject to disease and they grow taller than other animals. They were kept in a wooded, fenced area and fed alfalfa and commercial calf feed as well as weeds and bushes which were in their pasture. The age of the goats at operation varied from 4 weeks to about 3 months. Sixteen goats were used.

Selective cordotomy was done upon 1 of the goats. A femoral nerve section also was done upon only 1 goat. Upon 7 goats a sciatic nerve section about 1 cm. below the sciatic notch was done and a portion of the nerve was excised. Upon the remaining 6 goats anterior nerve root sections were done at the levels of the fourth and fifth lumbar and the first and second sacral vertebrae.

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TABLE NO. I

Showing changes in weight of muscle and length of bone

Goat	Procedure	Total Weight of Muscle in Grams		Total Length of Bone in Centimeters		Length Discrepancy in Centimeters
		Affected	Unaffected	Affected	Unaffected	
1	Femoral nerve section	841	932	36.6	36.4	+0.2
2	Sciatic nerve section	2164	2324	65.5	66.5	−1.0
3	Sciatic nerve section	2155	2454	66.2	67.0	−0.8
4	Sciatic nerve section	484	585	56.4	56.6	−0.2
5	Sciatic nerve section	553	649	56.5	57.1	−0.6
6	Sciatic nerve section	936	939	57.8	58.4	−0.6
7	Sciatic nerve section	450	571	59.6	59.4	+0.2
8	Anterior nerve root section	641	675	56.7	56.8	−0.1
9	Anterior nerve root section	716	717	59.5	60.2	−0.7
10	Anterior nerve root section	379	483	53.8	55.0	−1.2
11	Anterior nerve root section	554	946	57.1	57.8	−0.7

After a period of about one week the goats were able to feed and water themselves. They then were returned to the country where they were kept in a large fenced area and allowed to lead a normal existence. Four goats died in the postoperative period. One death followed a selective cordotomy, 2 died after anterior nerve root sections, and one death followed a sciatic nerve section. Sufficient time had not elapsed and sufficient growth had not taken place following operations upon these 4 animals to make it worth while to include them in this report.

Most of the goats had a slight limp after operation which was more evident when they ran. The most obvious defect in their activity was their inability to stand on their hind legs and feed from the trees as well as normal goats. Each of those having the sciatic nerve sectioned walked on the dorsum of the foot. Sores or trophic disturbances were not noted. In only 1 goat was there a significant disability and this was goat number 11. A 90 degree contracture at the hip and a 70 degree contracture at the knee developed. This has been shown by Sherman to occur frequently.[5]

When the goats attained maturity they were killed. The individual muscles of both lower extremities were examined and weighed. The length of each bone in the extremities was determined. These individual measurements are not included in this report because they failed to reveal anything more than did the total bone length and muscle weight (table I).

COMMENT

The greatest difference in limb length was 1.2 cm. which was not considered statistically significant. The average loss of length was less than .5 cm. The amount of muscle weight loss was not usually great but in goats numbers 1, 4, 5, 7, 10, and 11 there was a significant loss of muscle weight without comparable loss of bone length.

SUMMARY AND CONCLUSIONS

A partial nerve paralysis of the lower extremity has been produced in 16 young goats. Four goats died early in the experiments and are not included in the results. In this series no striking difference was noted in the length of growth of the hind limbs of goats following peripheral denervation.

No correlation between loss of motor innervation of a degree not producing complete paralysis or severe disability and length growth has been noted.

Additional studies should be made with more extensive peripheral denervations.

ACKNOWLEDGMENT

The authors express their gratitude to Dr. James B. Weaver for his help and encouragement in this project, and for providing us with a suburban pasturage for the goats.

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MANAGEMENT OF INTRACRANIAL ANEURYSMS OF THE ANTERIOR COMMUNICATING ARTERY*

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The syndrome of spontaneous subarachnoid hemorrhage is a common one, is readily diagnosed clinically, and is well understood. It usually is due to a ruptured intracranial aneurysm which frequently can be visualized by percutaneous arteriography. Once the lesion is demonstrated, decision must be made between ligation of the carotid artery in the neck, direct intracranial attack, or leaving the lesion alone and hoping recurrent rupture will not occur. The poor prognosis of nonsurgical management has been repeatedly stressed, so that most neurosurgeons believe that surgical treatment is not only justified, but indicated.

It is clear that many factors enter into the prognosis of these lesions, whether operated upon or not, and that statistical reports of aneurysms as a whole are difficult to interpret. Certainly the location of the aneurysm plays a great part in determining operability, and one of the most difficult sites to challenge the neurosurgeon is that of the anterior communicating artery. In this unique location, the aneurysm arises from, or replaces, a vessel usually only a few millimeters long, and often incorporates or encroaches upon one or both anterior cerebral arteries (fig. 1). It usually feeds from both carotid circulations, so that ligation of either carotid artery in the neck would only allow it to fill from the opposite side. In certain cases it fills only from one side due to deficiency, or absence, of the opposite anterior cerebral artery proximal to the anterior communicating artery, and in these cases both distal anterior cerebral arteries feed from one carotid circulation. In this type of variation, ligation in the neck would be disastrous since this would abolish the blood supply of both frontal lobes.

It is as yet unsettled whether aneurysms of the anterior communicating artery should be subjected to surgery. Reports in the literature are conflicting. Norlén and Barnum[5] recorded 24 surgical cases with only 4 deaths, and concluded that these aneurysms are best handled by direct intracranial approach. Graf[2] reported that of 10 cases of patients with these lesions who were operated upon, 8 died. Steelman, Hayes, and Rizzoli[7] stated that if the lesion is located on the anterior communicating artery and fills from both sides, surgery should not be attempted due to the danger of sacrifice of both anterior cerebral arteries.

Twelve consecutive patients who had aneurysm of the anterior communicating artery and were admitted to the University of Kansas Medical Center and the Veterans Administration Hospital in Kansas City, Missouri, are herein briefly reported.

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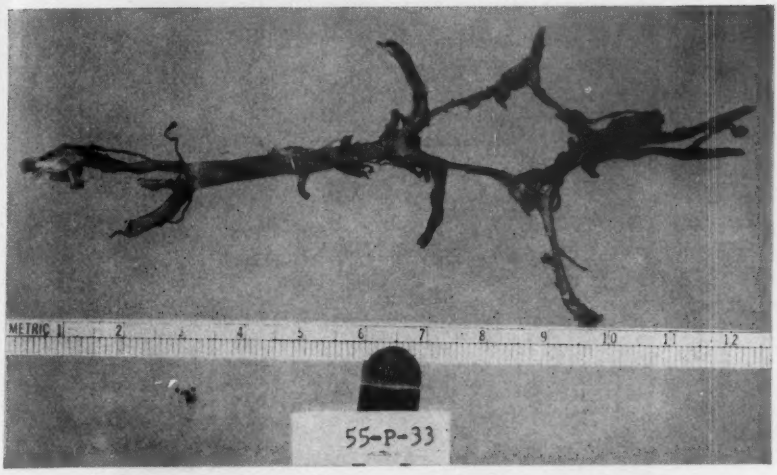

FIG. 1. Aneurysm of anterior communicating artery (case 7)

CASE REPORTS

Case 1. O. C., a 54 year old white woman, was admitted to the hospital one week after her initial subarachnoid hemorrhage. Before detailed investigation could be completed, she had a second massive hemorrhage. While she was in a critical condition, arteriography was done, and showed an anterior communicating aneurysm. Surgical exposure of the bleeding aneurysm was made four hours after the second hemorrhage, and due to difficult exposure and bleeding, it was eventually necessary to clip both anterior cerebral arteries to control the bleeding. This resulted in infarction of both frontal lobes, and death ensued three days later.

Case 2. Z. M. R., a 36 year old white woman, had three separate subarachnoid hemorrhages in one month. Arteriograms showed an anterior communicating artery aneurysm filling from both sides. Craniotomy was done 10 days after her last hemorrhage, and clipping of the right anterior cerebral artery and sac of the aneurysm was accomplished. The patient recovered, but had distinct personality impairment, and one year later still was mentally irresponsible.

Case 3. O. S., a 44 year old white man, was investigated 12 days after his initial subarachnoid hemorrhage. His anterior communicating artery aneurysm filled from both sides (fig. 2). At operation, the lesion was satisfactorily exposed without rupture. In this case, the ideal technical solution was accomplished, in that a Cushing clip was placed on each side of the aneurysm on the anterior communicating artery, and neither clip incorporated either anterior cerebral artery. This totally isolated the aneurysm from its circulation and preserved normal blood flow through both anterior cerebral arteries. However, 30 minutes after the wound was closed, the patient suddenly went into a peculiar decerebrate state, and the wound was re-explored. No postoperative clot or visible explanation for his condition was found. He promptly recovered from this complication to be left with a spastic weakness of the right leg only, which has remained permanent. Postoperative arteriograms (fig. 3) verified patency of both anterior cerebral arteries and complete obliteration of the aneurysm. We have no explanation for this residual neurologic deficit other than transient spasm of the left anterior cerebral artery, which definitely was not ligated.

Case 4. H. G., a 44 year old white man, was admitted to the hospital one day after his

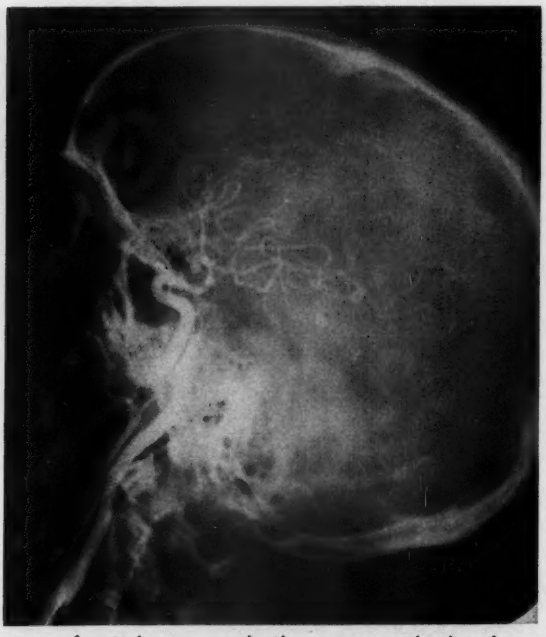

FIG. 2. Aneurysm of anterior communicating artery projecting downward (case 3)

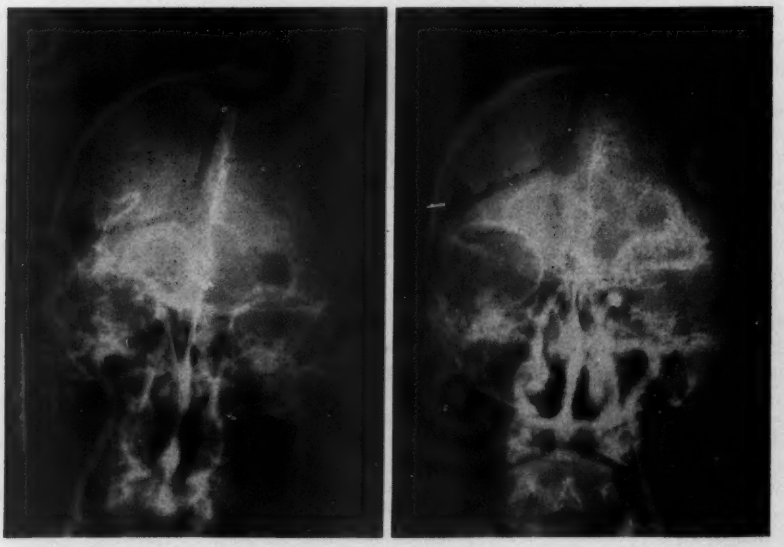

FIG. 3. Postoperative right and left carotid arteriograms showing obliteration of aneurysm and preservation of both anterior cerebral arteries (case 3).

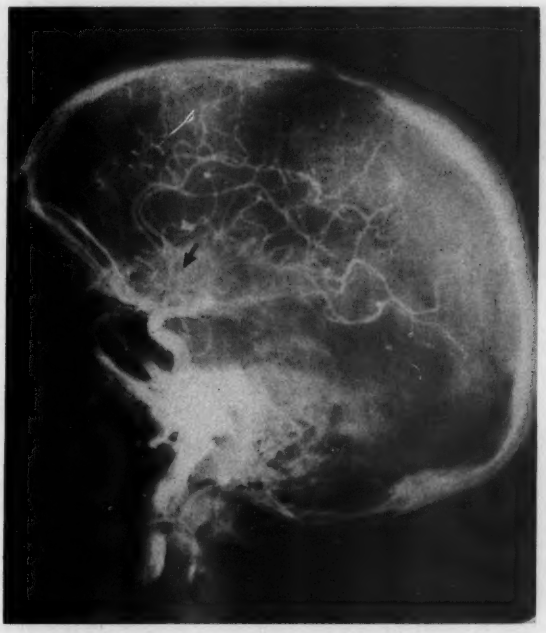

FIG. 4. Aneurysm of anterior communicating artery projecting upward (case 6)

second subarachnoid hemorrhage, the first having occurred eight days previously. Arteriograms showed a rather large aneurysm of the anterior communicating artery, which, in the oblique view (fig. 5), appeared to incorporate both anterior cerebral arteries. Craniotomy was done 11 days later, and in spite of hypotensive anesthesia, the lesion ruptured during its exposure. Clipping of the right anterior cerebral artery proximal to the lesion did not stop the flow of blood, but a second clip placed on the aneurysm itself did. The patient did not respond postoperatively, and died three days later. Autopsy disclosed severe generalized edema of the brain but no focal infarction of either frontal lobe.

Case 5. V. V. W., a 27 year old white man, had two subarachnoid hemorrhages and remained in a critical state after the second one. Because clinically it was thought that the lesion was still leaking blood, arteriography and craniotomy was done five days after the onset of the second hemorrhage. At operation, the left anterior cerebral artery proximal and distal to the lesion was clipped, as well as the anterior communicating artery between the aneurysm and the right anterior cerebral artery. The sac of the lesion also was clipped. The patient did not improve, and died six days later. Autopsy showed intraventricular hemorrhage which had been present from the time of the second rupture.

Case 6. S. B., a 51 year old white woman, was admitted to the hospital for investigation of a single subarachnoid hemorrhage. Arteriography showed an anterior communicating artery aneurysm (fig. 4) filling only from the left side. There was no right anterior cerebral artery proximal to the anterior communicating artery, so that both anterior cerebral arteries distal to the communicating artery fed entirely from the left side. Oblique roentgenograms showed that both anterior cerebral arteries appeared to be incorporated in the lesion. This aneurysm was thought to be too dangerous for surgical approach, and the patient was dismissed from the hospital completely recovered from her subarachnoid hemorrhage. She has not bled in the subsequent three months.

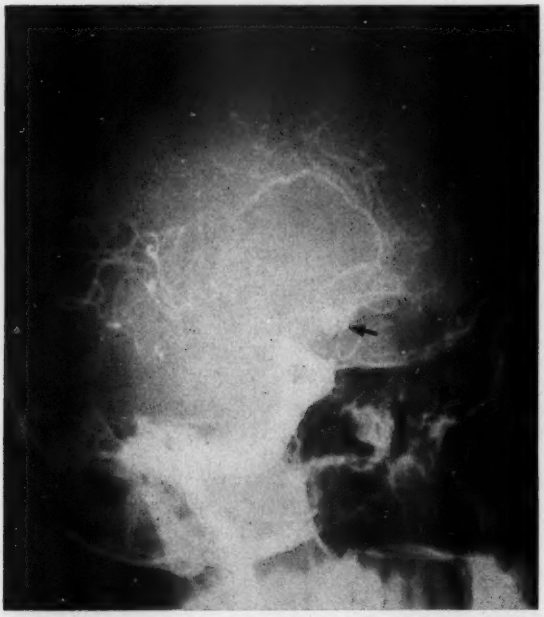

FIG. 5. Aneurysm of anterior communicating artery as shown in oblique view (case 4)

Case 7. W. W., a 42 year old Negro man, had two spontaneous subarachnoid hemorrhages and died in his second one before arteriography was done. At autopsy, a pedunculated aneurysm (fig. 1) of the anterior communicating artery was disclosed, which technically probably could have been ligated or clipped at its neck, preserving the circulation of both anterior cerebral arteries.

Case 8. C. S., a 22 year old white man, had one subarachnoid hemorrhage and was hospitalized and operated upon elsewhere. He was subsequently admitted to the Veterans Administration Hospital here for further opinion. The right anterior cerebral artery had been clipped, and the lesion was still present and filled from the left side. No further surgery was done.

Case 9. C. M., a 30 year old white man, had three subarachnoid hemorrhages. Arteriograms showed multiple aneurysms, one of which was on the anterior communicating artery, and another lobulated one on the left middle cerebral artery. He also had a persistent carotid-basilar anastomosis.[4] He remained in critical condition following his third hemorrhage, and died without surgical intervention.

Case 10. G. O., a 29 year old white man, was subjected to operation 10 days after his initial hemorrhage. His lesion filled from both sides, and at operation the anterior communicating artery as well as the sac of the aneurysm was successfully clipped without ligation of either anterior cerebral artery. The patient remains well and neurologically intact.

Case 11. G. T., was explored surgically four weeks after his single subarachnoid hemorrhage. Arteriography had shown no left anterior cerebral artery proximal to the anterior communicating artery. An anterior communicating aneurysm was present, and both anterior cerebral arteries filled only from the right. At operation, rupture of the lesion occurred which required clipping of the right anterior cerebral artery as well as the lesion itself. Although the patient still survives, he is a permanent inmate of a mental institution.

Case 12. L. P., a 55 year old Negro woman, had one previous subarachnoid hemorrhage

and three additional ones while hospitalized under our observation. Her fourth one had resulted in a left hemiplegia and marked mental dulling. Since our previous experiences had been very discouraging, this seemed to be a proper candidate for a new approach.

Under hypothermic anesthesia, with the patient's temperature at 85 F., surgical exposure of the chiasmal region was made. Both anterior cerebral arteries proximal to the anterior communicating artery were first deliberately exposed before approaching the aneurysm itself. Removable Olivecrona clips with wings[6] were placed on each, without tightly crushing the vessel. The aneurysm and the anterior communicating artery then were easily dissected out, and a small clot fell out of the blown-out end of the aneurysm. With no blood in the lesion, it was a simple matter to fully mobilize it, identify its exact point of origin in relation to the anterior cerebral arteries and anterior communicating artery, and to decide what type of clipping or ligation would be required. In this patient, the aneurysm arose from the crotch between the anterior communicating artery and the left anterior cerebral artery. It was cured by placing two clips on the neck of the sac, not incorporating the left anterior cerebral artery, and another on the anterior communicating artery medial to the right anterior cerebral artery. An unfortunate complication, unrelated to the aneurysm itself, occurred which resulted in having to permanently occlude the left anterior cerebral artery. A small anomalous ophthalmic artery was present, arising from the left anterior cerebral artery proximal to the anterior communicating artery. In the dissection of the left anterior cerebral artery from the dense adhesions due to previous hemorrhage, this anomalous vessel was inadvertently avulsed from the wall of the left anterior cerebral artery, leaving no stump to clip or coagulate. The temporary Olivecrona clip was placed over the bleeding site, and when later released, the vessel continued to bleed and required permanent clipping of this vessel.

The clip was removed from the right proximal anterior cerebral artery 11 minutes after its application. Had it not been for the torn ophthalmic artery, the temporary clip could have been removed from the left proximal anterior cerebral artery at the same time. This would have left the aneurysm cured, with both anterior cerebral arteries patent. It is evident that without hypothermia and proximal occlusion of all blood flow, such a thorough dissection and selective clipping would have been impossible.

Three weeks postoperatively, her poor preoperative neurologic status remains relatively unchanged.

DISCUSSION

Of these 12 patients, 7 had had multiple hemorrhages, verifying the tendency of spontaneous subarachnoid hemorrhage to recur, and emphasizing the poor prognosis of conservative management. Bilateral percutaneous carotid arteriograms were done in all but 1 patient, and vertebral arteriograms were done in only 2. Filling of the aneurysm from both sides occurred in 6, from the left side only in 4, and from the right side only in 1. Oblique roentgenographic views taken in three instances distinctly aided in preoperative interpretation of the relationship of the aneurysm to the anterior cerebral arteries. No complication from arteriography was noted.

In 2 patients, the aneurysms were multiple. Two aneurysms projected up, two down, four directly forward, three up and forward, and one down and forward. Nine patients had no localizing neurologic signs, and three had hemiparesis and mental changes.

Eight of the 12 patients were operated upon. Of these, 3 died postoperative, 2 having been explored in the critical bleeding stage. In each, the aneurysm ruptured at operation, and one or more anterior cerebral arteries had to be

sacrificed. Of the 5 who survived operation, 1 is permanently hospitalized in a mental institution, 1 is at home but mentally irresponsible, 1 is working with a spastic right leg, 1 is still hospitalized with a hemiplegia, and 1 is well with no residual deficit.

Of the 4 patients not operated upon, 2 have died and 2 have left the hospital neurologically intact. We have no word of subsequent hemorrhage in either.

Hypotensive anesthesia was used in 4 patients, and in 3 of them did not prevent rupture of the aneurysm as the dissection to expose it was begun. Of the 8 exposed surgically, 5 ruptured, and of these, 3 died.

It seems clear that good surgical exposure of the aneurysm with complete isolation of both anterior cerebral arteries proximal and distal to the lesion must be accomplished in order to destroy the lesion without occluding either anterior cerebral artery. It also is apparent that if the lesion ruptures, this type of deliberate exposure is difficult, if not impossible. It is evident in our small series that rupture of the lesion during the dissection, before adequate exposure is obtained, is to be expected, and that hypotensive anesthesia is not certain insurance against this disconcerting occurrence.

It thus seems logical that the answer to this problem lies in total temporary occlusion of all blood flow to the lesion during its isolation, and then placing of definitive clips or ligatures on the aneurysm in a bloodless field. This concept has been suggested by Campbell and Burkland[1] who used a silk noose, without hypothermia, in dealing with aneurysms of the middle cerebral artery. Both anterior cerebral arteries can be readily exposed through a unilateral frontal craniotomy, and temporarily occluded before the lesion itself is visualized. This guarantees no rupture or bleeding during the dissection of the lesion.

To allow more time for the definitive treatment of the aneurysm, hypothermia seems appropriate. Lougheed, Sweet, White, and Brewster[3] record a case in which the patient, under hypothermia, tolerated total occlusion of both carotid and both vertebral arteries for 14 minutes and 25 seconds without clinical evidence of brain damage from cerebral anoxia. Our last patient was thus treated surgically under hypothermia with temporary occlusion of blood flow to the lesion. The exposure was excellent, and the deliberate complete isolation of the lesion and ease with which it could be handled and obliterated was a pleasant and striking experience compared to our former battling with blood and exposure. One cannot draw any conclusion from only 1 case, but certainly further similar attempts seem justified.

SUMMARY AND CONCLUSIONS

Twelve consecutive cases of aneurysm of the anterior communicating artery are recorded. Eight patients were operated upon with 3 deaths, and 4 were left alone with 2 deaths. This series is too small to draw any conclusion other than that aneurysms of the anterior communicating artery are treacherous, whether operated upon or not.

In the acute bleeding stage, surgery is contraindicated.

In spite of hypotensive anesthesia, rupture of the lesion at the time of opera-

tion is the greatest cause of mortality and morbidity, because it obscures the surgeon's vision and usually results in surgical ligation of one or both anterior cerebral arteries. This complication can be avoided by deliberate temporary occlusion of both anterior cerebral arteries proximal to the aneurysm, using hypothermic anesthesia to prevent damage from the temporary cerebral anoxia.

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HYPERTROPHIC PYLORIC STENOSIS: A CLINICAL ANALYSIS OF EIGHTY-SEVEN CASES WITH SPECIAL REFERENCE TO ETIOLOGIC FACTORS*

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The operative procedure devised by Fredet and later modified by Ramstedt shortly after the turn of the century is still used almost universally in the treatment of hypertrophic pyloric stenosis. The mortality rate from this procedure has decreased steadily and is below 5 per cent in most recent series, with reports of as many as 225 consecutive cases of patients who were operated upon without a death.[12]

Although the surgical treatment of hypertrophic pyloric stenosis is highly successful, the cause is still unknown. In fact, it is not known whether the lesion exists prior to birth or begins in the neonatal period. In support of the view favoring the development of the mass prior to delivery are reports of stillbirths with hypertrophic pylori,[18] patients operated upon shortly after birth with operative findings of a tumor,[13, 14, 16] and the fact that this condition is frequently seen in premature infants.[20] Evidence favoring the development of hypertrophic pyloric stenosis after birth, however, is easily found in the literature. Wallgren[23] in Stockholm made upper gastrointestinal roentgenograms of 1000 consecutive newborn male infants with normal findings. Later 5 of this group developed signs and findings of pyloric stenosis. McKeown and associates[15] reported that of his patients operated upon before the age of 3 weeks, one-fourth of the number (a high figure) had no tumor at operation. They quote Meuwissen and Sloof[17] who reported an operation upon a child 2.5 weeks of age in whom the pylorus "was perhaps a little thicker than normal". Recurrence of symptoms led to another operation 35 days after the first and a very large tumor was found.

In an effort to determine prenatal and postnatal factors which may have some influence on the occurrence of this condition and to study clinical and operative findings and results, the records of all patients discharged from the University of Kansas Medical Center with a diagnosis of hypertrophic pyloric stenosis during the 10 year period ending Jan. 1, 1954, were reviewed and form the basis of this report. There have been 92 such patients, and of this number 87 have had the diagnosis proved at operation in this hospital. The remaining 5 patients are deleted from our analysis because they were not proved cases of pyloric stenosis while in our hospital. Follow up of these 5 patients showed that 1 died before operation and had no autopsy, 1 was treated medically and lost to follow-up at age of 5 months but was symptom-free at that time; another was treated medically and apparently was developing satisfactorily at last report; and 2 were operated upon at other hospitals with findings consistent with hypertrophic

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TABLE I

Age at onset of symptoms

Age in Weeks	Number of Cases
0 (at birth)	8
0–1	1
1–2	8
2–3	19
3–4	26
4–5	11
5–7	11
9–11	2
	86*

* Age not stated in 1 case.

pyloric stenosis. Thus, of 92 patients with a discharge diagnosis of hypertrophic pyloric stenosis, 89 have had surgical treatment, 1 died without operation, and 2 improved without surgery. There is some reason to doubt the diagnosis of pyloric stenosis in the 3 patients who were not operated upon, because of atypical clinical histories and the absence of palpable abdominal masses.

Only the 87 patients with diagnosis proved by operation at this hospital are included in this study.*

ETIOLOGIC CONSIDERATIONS

1. *Sex.* Hypertrophic pyloric stenosis occurs more frequently in males than in females. Various reports in the literature list the percentage incidence in males as 78 to 87 per cent.[1, 2, 5, 6, 25, 27] In this series of 87 patients, 78 per cent were males, a ratio almost identical to that reported at this hospital by Fredeen, Orr, and Neff in 1939.[9]

2. *Race.* Of the 87 patients, 89.6 per cent were white and 10.4 per cent were Negro. This figure is not significant because of disproportion between white and Negro admissions to this hospital. Ladd and associates[12] observed no racial predisposition in their series of 380 patients.

3. *Age.* The age at onset of symptoms varied between birth and 10 weeks. In 8 patients vomiting became apparent at birth or shortly thereafter, often manifested only by "spitting up" or regurgitation, which later became projectile in nature. The average age at onset of symptoms was 2.87 weeks. In 75 per cent of the patients, initial symptoms appeared in the second to fourth weeks, as is noted in table I. The average age at the time of admission to the hospital was 5.96 weeks.

4. *Birth Rank.* Primogeniture has been given etiologic significance by many authors on this subject. Ford, Ross and Brown[8] indicated the importance of this

* Inasmuch as at least half of these infants were operated upon by Dr. T. G. Orr, Sr., we wish to thank him for the use of his cases and for his generous assistance in the analysis of the data.

TABLE II

Birth rank

Rank	Number of Cases
1st child	25
2nd child	28
3rd child	17
4th child	2
5th child	2
	74*

* Rank not given in 13 cases.

factor in their study of 405 cases of hypertrophic pyloric stenosis. Of the hypertrophic pylorus patients born in Toronto, 51.8 per cent were first-born as compared to 41.2 per cent of the normal infant group, a difference which was shown to be statistically significant. In other series the percentage of first-born patients has ranged from 39 to 74 per cent.[2, 6, 12, 19, 27] It is pointed out by Delprat and Pfleuger[4] that the average American family has 1.5 children; 66 per cent therefore are normally first-born and "there is therefore no evidence at all to support the statement that pyloric stenosis is a disease of the first-born." Of the 74 patients in our series for whom birth rank data is available 33.8 per cent were first-born, as noted in table II. Actually more of these patients were second-born than were first-born. These findings detract from the significance of primogeniture as an etiologic factor in hypertrophic pyloric stenosis.

5. *Prenatal Influence.* Of the 83 patients with available maternal prenatal history, only 6 showed deviations from normal, as listed in table III. No consistency is seen in these factors and with the small percentage of patients in this list prenatal influence has no etiologic significance. It should be mentioned that in no mother was polyhydramnious observed. This condition is seen most frequently when fetal congenital abnormalities are present, especially obstructive

TABLE III

Significant prenatal history

Condition Recorded in Mother's History of Pregnancy	Number of Cases
4-plus serology	1
Hematuria and ankle edema last 2 months gestation	1
Vomiting and bleeding at 2 months gestation	1
Anemia throughout pregnancy	1
Bleeding 2 weeks before delivery	1
Influenza at 2 months gestation	1
	6*

* In 77 cases pregnancy was recorded in the charts to have been normal. In 4 cases no history concerning the pregnancy was available.

TABLE IV

History of delivery

Information Available Concerning Delivery	Number of Cases
Normal delivery	68
Breech presentation	3
Outlet forceps delivery	2
Hard or prolonged labor	2
Cesarean section	5
Infant cyanotic 2 days after birth	1
Twins delivered	2*

* One set monovular twins, one set binovular. In neither set of twins did the second twin develop hypertrophic pyloric stenosis.

lesions of the esophagus and upper intestinal tract, and might be expected in hypertrophic pyloric stenosis were the stenosis congenitally present.

6. *Gestation Period.* The gestation period was complete in 75 of the 82 patients on whom this information was recorded. Four patients were delivered at 7.5 months, 2 at 8 months, and 1 at 8.5 months. This factor also has no apparent importance in the etiology of pyloric stenosis.

7. *Delivery.* Birth trauma has been suspected by Flynn[7] as a predisposing factor in hypertrophic pyloric stenosis. Of 83 patients in our series with birth data available, 68 reportedly had a normal delivery. Births other than normal are listed in table IV and constitute only 18 per cent of the total group. No consistency is seen in the type of birth abnormality nor was specific infant trauma indicated in any patient. The reasons for Cesarean section were varied.

8. *Family History.* Numerous reports in the literature mention that there is a familial tendency for the development of hypertrophic pyloric stenosis.[2, 11, 21] The frequency of occurrence in both monovular twins and two or more siblings also has been reported many times.[24, 26] Bendix and Nicheles[3] report a high incidence of nervous disturbances in adult patients who had Ramstedt operations in infancy and in their families. These authors submitted a theory of autonomic imbalance as a cause of hypertrophic pyloric stenosis. Of the group of 87 patients under consideration, it is noted in table V that there were incidences of hypertrophic pyloric stenosis or infantile vomiting in the families of only 5. The other family illnesses listed are few and are of no etiologic importance.

9. *Feeding.* It has been recorded that hypertrophic pyloric stenosis predominates in breastfed infants[25] and for this reason feeding histories were tabulated in 82 patients in whom this data was given. Of this number 50 patients (61 per cent) received formulas of various types, 27 (33 per cent) were both breast and formula fed, and only 5 (6 per cent) were entirely breast fed.

A summary of the etiologic factors studied shows that hypertrophic pyloric stenosis predominates in male infants without racial predisposition. The importance attributed in other reports to primogeniture is not borne out in this study, in that more of these patients were second-born than first-born. Prenatal maternal illnesses, length of gestation period, and birth trauma have no ap-

TABLE V

Family history

Condition Recorded	Relationship	Number of Cases
Pyloric stenosis	cousin	1
Pyloric stenosis	brother	1
Vomiting shortly after birth, subsiding spontaneously	sister	
Vomiting in infancy, spontaneous recovery	siblings	2
Vomiting shortly after birth, responding to "thick feedings"	uncle	1
Hepatitis following delivery	mother	1
Stillborn sibling	sibling	1
Hay-fever	mother	1
Chorea	mother	1
Brain tumor	mother	1

parent significance in the incidence of hypertrophic pyloric stenosis. Likewise, the type of feeding in the postnatal period does not influence the development of the lesion. The factor of heredity is not shown to have great importance as an etiologic factor in this series of cases.

SYMPTOMS

The chief symptom in all 87 patients who had hypertrophic pyloric stenosis was vomiting. Vomiting was described as projectile in nature in 82 per cent of the patients. The presence of bile or yellow coloration of the vomitus was not observed in any patient, a point of importance in differentiating this condition from duodenal stenosis or band obstruction, where the vomitus usually does contain bile. Blood streaks were noted in the vomitus of 2 infants.

Other symptoms and their incidence of occurrence are listed in table VI. The

TABLE VI

Symptoms of hypertrophic pyloric stenosis

Symptom		Number of Cases
Vomiting:		
Projectile	71	
Nonprojectile	16	87
Constipation or decreased numbers of stools		53
Loss of weight or failure to gain		50
Peristalsis (noted by parent)		17
Decreased urine output		13
Diarrhea		5
Irritable		4
Lethargy		2
Convulsions		2
"Cried as if in pain"		2
Increased borborygmus		2
Miscellaneous		7

majority of patients were noted to have decreased numbers of stools and loss of weight or failure to gain weight. Decreased urinary output was noted by parents in 13 patients. Abdominal peristalsis was observed in 17 patients.

PHYSICAL FINDINGS

Admission physical findings and their incidence are listed in table VII. The presence of an abdominal mass was noted on physical examination in 80 per cent of the patients and was questionably palpable in an additional 7 per cent. This is comparable to the 76 per cent with palpable tumor reported by Akin and Forbes.[1] The presence or absence of a mass is the most important physical finding in the diagnosis of this condition. In the absence of a mass, roentgenologic studies are indicated and are most helpful in establishing the correct diagnosis. All masses were clinically palpable in the right upper quadrant except 3 in the midline, 1 to the left of the midline, and 1 just above the right inguinal ligament. Descriptions of the sizes and shapes of the masses varied from a *"pea"* to a *"golf ball"*, but the most common descriptive term used was *"the size of an olive"*. Upper abdominal peristaltic waves were visible upon physical examination in more than 75 per cent of the patients. These could be produced easily by allowing the infant to swallow a small quantity of feeding.

There were recorded impressions of weight loss on physical examination in 44 instances. Comparison of admission weights with birth weights in 74 patients in whom this data is available showed that 47 had gained weight (an average of 477 grams) and 27 had lost weight (an average of 334 grams). This represents an average gain of only 181 grams over birth weight at the average of 6.3 weeks for all 74 patients. A minimum normal gain of 945 grams would be expected at this age.[10]

Evidence of dehydration was present in 53 patients, and skin turgor was noted to be abnormal in 34. Fifteen infants were lethargic as a result of extreme fluid

TABLE VII

Physical findings

Finding		Number of Cases
Abdominal mass:		
Palpable	70	
Questionably palpable	6	76
Visible peristalsis		67
Dehydration		53
Evidence of weight loss		44
Abnormal skin turgor		34
Lethargy		15
Sunken fontanelle		5
Inguinal hernia		2
Abdominal distention		2
Irritability		2
Miscellaneous		11

and electrolyte losses. A sunken fontanelle in 5 patients was another manifestation of dehydration and decreased blood volume.

Only 2 patients showed significant temperature elevation on admission.

Accompanying congenital anomalies were few in this series, with only one congenital heart defect and two inguinal hernias being found. The low incidence of congenital anomalies associated with this condition has been referred to by Akin and Forbes[1] and is further evidence against hypertrophic pyloric stenosis having a congenital anomalous etiology, since such malformations frequently are multiple.

It has been mentioned by Schwartz and associates[20] that symptoms of hypertrophic pyloric stenosis in premature infants may present somewhat atypical symptoms. The 7 premature infants in this series, whose gestation periods have been listed in a previous section, were studied as a group. The symptoms were the same in these as in the full-term infants studied, and an abdominal mass was palpable in 5 of the 7. The average age at onset of symptoms was 3.3 weeks in the premature infants which does not differ significantly from the average of 2.87 weeks in the total group.

PREOPERATIVE CONSIDERATIONS

Donovan, as early as 1932, pointed out that "preoperative preparation is perhaps the most important factor in lowering the operative mortality in these patients."[5] During the past 10 years there has been an increasing trend at this institution to devote more time preoperatively to the correction of fluid, blood, and electrolyte deficiencies. In the period of 1944 to 1946 the average period of hospitalization prior to operation was 2.4 days. In 1952 and 1953 this period was 3.4 days. All of the 87 patients in the cases here reported received parenteral fluids preoperatively and 52 received whole blood some time during their hospital stay. Dehydration apparently was not an important factor in the deaths reported in this series whereas in the series previously reported from this institution dehydration and starvation probably were important factors.[9] Todd mentions that severe dehydration was present in 11 of 12 deaths in his series of patients treated medically.[22]

OPERATIVE FINDINGS

The extramucosal Ramstedt pyloromyotomy was used in all 87 patients in this series. A Finney pyloroplasty also was done in 1 patient in whom the pyloric area was atypical in that two pyloric rings and a partial duodenal membrane were present. In addition, in 13 patients, a biopsy of the pyloric musculature was taken for future study by making an incision in the pylorus parallel to the primary incision. A pyloric tumor was found at operation in all 87 patients. The lesion was typically olive shaped in all but 3 patients. In 1 of these the tumor was not uniform in circumference, 1 had aberrant pancreas on the anterior surface of the duodenum, and the other had two pyloric rings with a partial duodenal membrane as mentioned above. Although these atypical findings suggest lesions

other than hypertrophic pyloric stenosis they are retained in the series because the operating surgeons so classified them.

It has been stated by McKeown and associates[15] that the size of the tumor is highly correlated with the age at operation in his series of 578 patients who were operated upon. An attempt was made in 48 of our patients, with tumor size data available to compare age and tumor size; no significant correlation was noted. Tumor sizes ranged from 1 by 1 to 2 by 3 cm.

Inadvertent perforation through the mucosa by the myotomy incision occurred in 9 patients. This was recognized and closed in all patients and no morbidity or mortality resulted from this error. The danger of mucosal perforation lies in the failure to note its presence and allowing it to remain unclosed.

Bleeding from the myotomy incision was of insufficient quantity to require ligation or suture in 28 patients. One of the 2 deaths in the series was the result of unrecognized hemorrhage from the myotomy incision several hours after operation.

COMPLICATIONS

Postoperative vomiting occurred in 69 patients. The vomitus was small in quantity in most instances and diminished over the postoperative period, but continued for an average of 5.5 days. Projectile vomiting was observed postoperatively in only 1 patient. This patient was re-explored 13 days after the first Ramstedt operation with findings of incompletely divided muscle fibers in the myotomy incision. These were divided and the patient recovered uneventfully. In another patient nonprojectile vomiting continued for 12 days after the Ramstedt operation so the infant was re-explored. Since there was no evidence of pyloric obstruction at this operation the abdomen was closed without other procedure and after another 4 days of vomiting the infant recovered satisfactorily.

The only wound complications were three superficial infections, none of which was in a patient with duodenal perforation. No wound disruptions were encountered although several types of incisions were used by the several resident and staff surgeons.

Temperature elevations of 101 F. or higher were noted in 14 patients. One of these had inadvertent duodenal perforation with closure and 2 had wound infections. The cause of the temperature elevation was not apparent from examination of the records of the remaining patients.

Other complications, excluding the 2 deaths discussed in another section of this paper, included convulsions in 1 infant, presumably due to hypocalcemia, and diarrhea in 1.

POSTOPERATIVE HOSPITALIZATION

The average period of postoperative hospitalization was 10.1 days. Szilagzi and McGraw[21] reported an average postoperative stay of 14.8 days in their series in 1943. The average weight gain after operation prior to dismissal was 286 grams in our series, which represents a normal gain for this period.

DEATHS

Two deaths occurred, both on the day of operation. This represents 2.3 per cent of the 87 patients. One, a premature infant, died with the clinical signs of cyanosis and dyspnea and postmortem examination showed atelectasis and pneumonitis to be present. The other died of unrecognized hemorrhage from the myotomy site.

RECOMMENDED MANAGEMENT

In most cases of hypertrophic pyloric stenosis, the correct diagnosis can be made from the history and physical examination only. However, when an epigastric mass is not palpable, or for other reasons the diagnosis is in doubt, roentgenologic studies, using a small quantity of thin barium, should be obtained. Prolonged gastric retention of the barium with hyperperistalsis are characteristic roentgenologic findings in this condition. A "*rat-tailed*" deformity of the pylorus usually is observed. Upon completion of the examination, excess barium should be aspirated from the stomach.

Parenteral fluids and electrolytes must be given as needed to correct dehydration and electrolyte imbalance prior to operation. Serum chlorides ranged below 70 mEq./L in 5 patients. Plasma and whole blood may be necessary to combat deficiencies in blood volume and hemoglobin deficiencies. After adequate fluid replacement, as judged by clinical and laboratory findings, early operation is advised. In the rare cases when the patient has extreme dehydration and aspiration pneumonia early operation under local anesthesia, after a short period of preparation, is indicated.

Using general anesthesia, a small right upper quadrant transverse muscle splitting incision is made to obtain adequate exposure to permit grasping the pyloric tumor. After delivering the tumor into the operative field the serosa overlying the tumor is incised carefully and the remaining muscle layers spread with a curved hemostat. The mucosa should bulge into the incision. If mucosal perforation should occur immediate closure with a fine suture is done. Any bleeding points which persist after a short period of sponge pressure are best ligated or sutured. The abdomen is closed in layers with fine nonabsorbable interrupted sutures.

Water is given in small quantities orally 12 hours after operation and if this is well tolerated the quantity and formula additions are increased gradually until full strength formula is being taken in normal quantities. Parenteral fluid supplements are given as required to maintain an adequate intake. Regurgitation of small quantities of feeding is to be expected in the early postoperative period.

SUMMARY

A study of the case reports of 92 cases of hypertrophic pyloric stenosis forms the basis of this study. Only 3 of these patients were treated medically and in none of the 3 was a pyloric tumor palpable.

Of the 87 patients treated surgically at this hospital 2 (2.3 per cent) resulted in death.

Seventy-eight per cent of the 87 patients were males.

The average age at onset of symptoms was 2.87 weeks and the average age at the time of hospitalization was 5.96 weeks.

About one-third of the patients in this series were first-born children. There were more second-born than first-born children.

Prenatal, birth, family and feeding histories revealed no information of etiologic significance.

Vomiting was the presenting symptom in 100 per cent of the patients.

An abdominal pyloric tumor mass was palpable in 80 per cent of the patients in this series.

Accompanying congenital anomalies were infrequent in the patients who were studied.

Inadvertent duodenal mucosal perforation occurred in 9 patients and it was necessary to suture bleeding vessels in the myotomy incision in 28.

Because of persistent symptoms 2 patients were operated upon a second time.

Recommendations of management of hypertrophic pyloric stenosis are presented.

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ACUTE CHOLECYSTITIS: AN ANALYSIS OF SIXTY-ONE CASES*

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Any discussion of the treatment of acute cholecystitis must take into consideration the physiology of that organ and of the liver. With these facts well in mind one must always use careful judgment in the treatment of the patient with this disease. Generally speaking there is no controversy about the fact that operation with removal of the gallbladder and/or any obstructions of the duct system is the proper treatment for acute cholecystitis. However, there still is a great divergence of opinion as to the time this therapeutic measure should be applied.

There are few clinical syndromes which tax the diagnostic ability and clinical judgment of a physician more than does acute cholecystitis. The term itself is rather ambiguous, as it is an all inclusive term, and is loosely used to include all pathologic conditions of the gallbladder from simple acute edema to gangrene and perforation. There are no definite criteria which reliably distinguish the various changes.

The disease usually begins with a rather typical attack of colic, which persists and becomes worse with signs of increasing infection. In nearly all instances there is a previous history of gallbladder disease with colic, often over a period of many years. However, occasionally a patient may be seen who develops an acute abdominal condition with the first attack of gallbladder disease.

The etiology of the disease is variable. The most common etiologic agent is an obstruction of the outlet of the gallbladder, most commonly due to a stone lodged in the cystic duct. Obstruction may occur, however, due to a number of other factors. Among these factors are the following: kinking of the cystic duct at its junction with the gallbladder, adhesions, adjacent periduodenitis, enlarged lymph nodes, and tumors in the immediate vicinity of the gallbladder or common duct. The obstruction produces an accumulation of secretions within the gallbladder, which, in turn, is followed by distention and subsequent compression of the vessels and lymphatics in the wall of the organ. Thrombosis of the cystic arteries even may be produced. At any rate an ischemia develops as the result of the impaired circulation and may be followed by necrosis, gangrene, and perforation. Nearly all experimental workers, as well as clinicians, are agreed that infection is a secondary phenomenon, inasmuch as most acutely infected gallbladders operated upon in the first 48 to 72 hours of the disease give a sterile culture of the gallbladder contents. Thomas and Womack[17] believe that an operation should be deferred after 48 hours have elapsed from the time of the onset of the symptoms. Goldman, Morgan, and Kay[7] studied the bacteriology of acute cholecystitis at the University of California, and found that there is an associated lower incidence of positive cultures during the first three days of the acute disease.

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From these studies they concluded that if operation is done during this time there is a lower mortality rate.

CLINICAL FEATURES

The clinical features of acute cholecystitis are of great interest. The disease may occur at any age of life, but it is primarily a disease of the fifth and sixth decades. Females predominate over males. Pain is the outstanding symptom, is severe, and often is not relieved by opiates. Nausea and vomiting usually occur. There is tenderness, most marked in the right upper quadrant, which is associated with muscle spasm, rebound tenderness, and at times even with rigidity. Jaundice occasionally is present. Lester[10] studied 109 cases and found that 17 per cent of the patients were jaundiced, but there were stones in the common duct in only 4.6 per cent. He believed that jaundice plus a dilated common duct demands exploration of the common duct because stones usually will be found, even if not felt. In other patients the jaundice is thought to be due to hepatitis, or to edema and there is inflammation about the common duct. Abdominal distention may occur. A mass may develop in the right upper quadrant, and this often increases in size and becomes increasingly tender as the disease progresses. There usually is an elevated temperature, and this may continue to rise. At the onset of symptoms the temperature often is in the neighborhood of 100 F. Leukocytosis generally occurs, and at the beginning averages about 11,000, but later may rise as high as 30,000 to 40,000 per cu. mm. in some patients with extremely severe disease. There usually is a concomitant rise in the pulse rate with the increase in the temperature. There may be impaired liver function, and the urine may contain bile. Roentgenologic studies in the acute stage should be confined to a scout film of the abdomen.

The disease may progress insidiously, or it may become fulminating almost immediately after the onset of symptoms. The complications which occur may develop early. According to Berk[1] these complications include: gangrene, perforation, empyema, generalized peritonitis, internal biliary fistulas, extension of pericholecystic abscess, pylephlebitis, cholangitis, pancreatitis, hepatitis, and septicemia.

DIFFERENTIAL DIAGNOSIS

It has been stated that many of the patients operated upon early are found not to have acute cholecystitis, but rather some other acute condition. Acute cholecystitis must be differentiated from the following: acute appendicitis, coronary disease, perforated peptic ulcer, acute pancreatitis, renal colic, pneumonia, pleurisy, intestinal obstruction, mesenteric thrombosis, hepatitis, internal hernias, intussusception, volvulus, pelvic inflammatory disease, tabetic crisis, herpes zoster, allergic reactions, common duct stones, and malignant lesions in or about the common duct. The history of similar attacks in the past, typical biliary colic pain, palpation of a tender distended gallbladder, fever, leukocytosis, and right upper abdominal tenderness and rigidity are all features that help one to make the proper diagnosis of acute cholecystitis.

TREATMENT

In the treatment of this disease there is no divergence of opinion among clinicians and surgeons that surgical intervention is necessary. However, the timing of operation is a subject of disagreement.

Those exponents of the *early operative* (emergency) method present excellent arguments for their thesis. They contend that the inability to predict the clinical course of a given patient, and in many instances the inability to recognize serious changes in the gallbladder make it imperative to operate early. They believe that there is less risk in operating than there is in waiting, inasmuch as there is eliminated the risk of the development of fatal complications. The high mortality rate in complicated cases is stressed. It is asserted that the edema present may even expedite the dissection of the gallbladder. Hospital stays are apt to be shorter, and postoperative complications are fewer.

Marshall and Phillips[12] state that "Acute cholecystitis is an acute surgical condition in which early operation, preferably within 48 hours after the onset of symptoms, permits a more thorough operation at less expenditure of time, money and suffering on the part of the patient as well as reduction in the operative risk. Early operation should reduce the mortality in the older age group as it lessens the hazards of depleted reserves in cases of concomitant disease".

Heyd[8] wrote in an editoral entitled "Acute Cholecystitis—Why Delay?" as follows: "The indication is to operate carefully with due celerity, relieve the mechanical obstruction, and provide drainage. Teachers of surgery who lend their prestige and give support to a policy of waiting provide authority for timid surgeons, inexperienced operators, and procastinating practitioners."

Pines and Rabinovitch,[15] in a study of 1480 patients operated upon for acute cholecystitis at the Brooklyn Jewish Hospital, found that the optimum time for operation often is missed, because the patient may not be seen until several days have elapsed after the onset of symptoms. In their series there were 90 perforations, with a mortality rate of 23.3 per cent, whereas in the uncomplicated cases of acute cholecystitis there was a mortality rate of 6.5 per cent. They maintain that the optimum time for operation is before the fourth day after the onset of symptoms. They state that "With adequate preparation of the patient, skillful anesthesia, precise surgery and knowledgeable postoperative management, it is possible to operate safely even on the very ill patients. The hazard lies rather in the delayed cases where technical difficulties surrounding the lesion increase the risk of operation".

Ross, Boggs, and Dunphy,[16] in studies made at the Peter Bent Brigham Hospital, indicate that resolution of the inflammatory process after an attack of acute cholecystitis is extremely slow and incomplete regardless of the clinical course of the patient. After a short period devoted to restoration of fluid balance and beginning antibiotic therapy, there is nothing to gain, they believe, by delaying operation if the patient is doing well. The inflammatory process persists for months and sometimes years. They maintain that the concept that there is any arbitrary critical period during which surgery for acute cholecystitis is to be avoided should be abandoned. In their series of patients the fourth to twelfth

days constituted the most lethal period, but they believe that this is due to the disease process usually reaching its peak of severity at this time rather than to whether operation is done or withheld during this period.

Glenn[6] also is an advocate of early operation. In a report of 555 patients operated upon for acute cholecystitis at the New York Hospital over a period of 14 years he found 17 patients who developed acute cholecystitis while convalescing from other surgical procedures.

Cole[4] believes that if the patient is seen within 48 hours after the onset of the symptoms emergency operation is justifiable.

Advocates of the *conservative or delayed surgical treatment* emphasize the fact that in most instances the disease will quiet down, and they contend further that the mortality rate is higher when the operation is done in the acute stage. They also stress the opinion that greater surgical skill and judgment are required when inflammation and swelling are present, as anatomic landmarks are often obliterated, and as a result there is more danger in damaging permanently the ductal system, and thus in turn producing a greater number of postoperative complications.

McGuigan,[11] in a study of 123 patients, stated that the mortality rate after delayed operation was 2.3 per cent as compared to 12.7 per cent after early operation. He therefore believes that delayed operation is the method of choice, but that operation must be done promptly if perforation of the gallbladder appears imminent.

Mustard and Custer[13] studied 211 patients seen over a 10 year period. Early operation was done in only 36 of these patients. These authors recommended aggressive conservatism, and reached the conclusion that any trend of thought is not sound which leads to increasing the popularity of difficult technical procedures done in dangerous areas possibly by untrained surgeons.

Freund,[5] in his study of 140 cases, recommends conservative waiting. He believes that many cases of acute cholecystitis could be eliminated by cholecystectomy before the acute attack strikes, inasmuch as an overwhelming majority of patients with acute cholecystitis give a previous history gallbaldder disease.

A third group of surgeons takes the middle course between the early and delayed surgical management of acute cholecystitis. These surgeons believe that each individual patient must be treated as a separate entity, and that no surgeon should be so unwise as to follow a fixed set of rules in the treatment of all patients suffering from acute cholecystitis. They also believe that in many instances if the findings when the patient is first seen indicate that perforation is imminent operation should not be delayed, but rather is mandatory, and must be done as soon as the patient's condition will permit. Fluid balance, electrolytes and vitamins must all be restored, and antibiotics must be instituted before this is done. Regardless of the decision to be made in each case, the patient should be hospitalized immediately when first seen so that he can be followed more readily, and if complications develop operation can be done without further delay. Those patients with signs of perforation and peritonitis, or with fever, rapid pulse, marked leukocytosis, a large tender gallbladder, increasing toxemia, and persistent pain

not relieved by morphine, suggesting imminent perforation need to be operated upon promptly. If the condition of the patient when first seen permits, and it often does, an initial conservative regime should be instituted. If in 24 hours his condition has not improved, and the disease still is showing progression, then further delay is not wise, and operation should be done at once. Buxton, Ray and Coller[3] are exponents of such a form of management. They studied 109 patients with acute cholecystitis at the University of Michigan Hospitals. These occurred in a group of over 7000 patients operated upon for extrahepatic biliary disease. They further advocate that the operation of cholecystostomy should be used much more frequently, with a subsequent cholecystectomy at a more optimum time. They believe that in view of the dangers of duct injuries associated with cholecystectomy when there are difficult anatomic and pathologic abnormalities accompanying acute inflammation of the gallbladder and bile ducts, one should seriously consider cholecystostomy as the operation of choice whenever the acute process may cause technical difficulties. They believe that a secondary cholecystectomy under more favorable conditions is a low price to pay for an intact duct system. Their indications for early operation include: failure of rapid and prompt regression of fever, leukocytosis and abdominal signs of acute inflammation under adequate and vigorous medical management, diabetes, severe cardiac and renal disease which are apt to be further burdened by severe infection, pregnancy, patients ill with serious complicating disease present prior to the onset of the acute cholecystitis, recurring acute cholecystitis, and unremitting jaundice.

TECHNIC

The technic of the operator in acute cholecystitis is very important. This is true because there often is so much distortion of the anatomic landmarks that it is difficult to identify the structures properly, and in inexperienced or careless hands damage of an irreparable character to the duct system may be done.

In surgery of the gallbladder, whether in an acute state or otherwise, the cardinal rules as outlined by Orr[14] in his "Operations of General Surgery" should always be kept in mind. These are: 1. Proper preoperative and postoperative care of patients saves many lives. This requires a thorough knowledge of the anatomy, physiology, and pathology of the biliary tract. 2. No gallbladder should be removed until the common hepatic duct, cystic duct, and common duct are identified. 3. Visualize and identify everything before cutting anything! If the surgeon will follow these principles at all times, even in acute cholecystitis, there would be many less damaged duct systems.

Lahey[9] always advocated that cholecystostomy, when avoidable, should not be done, as cholecystectomy in acute cholecystitis is by far the most satisfactory surgical procedure, and in the hands of men with experience, equipment, and good anesthesia it can be done safely in a great majority of patients. Sometimes, however, there are patients in whom it is desirable to do a cholecystostomy. Speaking of the technical difficulties and hazards, he advised that the gallbladder should always be approached in acute cholecystitis from above downwards. He

was of the opinion that, with the gallbladder freed from its bed in the liver, and with the shelving edge of the liver pulled up with a retractor, and with the neck of the gallbladder where the cystic duct enters the common duct and the hepatic ducts well exposed under a good light, there could be little chance of injuring the duct system.

Marshall and Phillips, Lahey, and others, are of the opinion that when stones are present in the common duct, and especially when there is an associated jaundice, that choledocholithotomy should be done. Cole has stated that, when jaundice is present, and a stone is palpable in the common duct, the duct should be opened and the stone removed. In acute cholecystitis any operative treatment which does not remove an obstruction of the common duct is poor therapy, and failure to do so may result in a fatality.

The operative mortality rate usually is higher in the older patients. This also is true of those with complicating disease, such as diabetes, according to Blumberg and Zisserman[2]. Heart disease and renal disturbances also are attended with a higher mortality rate. Perforation has a much greater mortality rate than the average. Cole has stated that to a great extent the mortality rate in any series will be strongly influenced by the number of free perforations into the peritoneal cavity, because the mortality rate is so high in this group, often being as great as 60 to 75 per cent.

Postoperative complications which are most commonly seen include: atelectasis, pneumonia, embolism, wound infection, abscesses, and the development of the so-called hepatorenal syndrome. The number of complications is apt to be less if the patient with this disease is operated upon during the first 48 hours of his illness.

The results in the treatment of acute cholecystitis are quite variable in the numerous groups of statistics available in the literature.

CLINICAL STUDIES

We are reporting the cases of a series of 61 patients operated upon for acute cholecystitis from our service in the Wichita Clinic during the period from 1948 to 1952 inclusive. These were consecutive cases of acute gallbladder disease occurring in 224 consecutive patients operated upon for extrahepatic biliary disease during this same period. We have not included any patients seen on our charity service at the Sedgwick County Hospital, or on our consulting service at the local Veteran's Hospital. This therefore represents an incidence of 27.2 per cent of pathologically proved cases of acute cholecystitis in the entire series of 224 patients. This group of 61 patients consisted of 40 females, ranging from 19 to 85 years of age with an average of 58 years, and of 21 males, varying from 25 to 84 years of age and with an average of 52.6 years.

Nearly all of these 61 patients gave a history of having had gallbladder trouble in the past, often over a period of many years. There were 7 patients with acute disease proved pathologically who had no stones at operation. Perhaps these might fall in the group who may have passed small stones prior to operation, although in several of these this did not seem likely.

Eleven, or 18 per cent of our patients in this group had jaundice, and of these 11 there were 9 in whom common duct stones were found at operation. This is at considerable variance with many groups of statistics, in which only about one-fourth of the patients with jaundice in acute cholecystitis were found to have common duct stones. In addition to the 9 jaundiced patients with common duct stones, 3 other patients were found to have common duct stones, which were removed at operation, making a total of 12 or 20 per cent of the entire group with common duct stones.

Perforation was found in 7 or 11.2 per cent of the patients, and of these 3 or 43 per cent died.

There were 2 patients, both males, who developed acute gangrenous cholecystitis while convalescing from other operations. One had had a spinal fusion, and the other had had the removal of a ruptured disk.

Internal biliary fistulas were found in 4 patients, an incidence of 6.56 per cent. There were two cholecystogastric, one cholecystocolic, and one cholecystoduodenal fistulas in this group.

The pathologic reports showed that there were 10 instances of gangrene, 7 of perforation, 7 listed as empyema, and 7 as acute suppurative cholecystitis (perhaps these last 2 groups should have been listed simply as 14 cases of empyema), and the remainder were diagnosed as acute, or as acute and chronic cholecystitis—usually with cholelithiasis. In 2 patients pericholedochal abscesses were found, 1 patient had multiple small liver abscesses, and in 1 patient a report was made of a distinct abscess in the gallbladder wall itself.

One patient was operated upon 9 hours after the onset of her symptoms of acute cholecystitis, which was accompanied by violent vomiting and straining. Soon after the onset of pain she developed a strangulated ventral hernia with complete obstruction of the ileum.

The period of time which elapsed between the onset of symptoms and operation in this series was quite variable, and illustrates the fact that we are inclined to individualize each patient with this disease, and try to treat each one on its own merits.

There were 24 patients operated upon under 4 days from the onset of symptoms, or 40 per cent of the entire group of 61 without a death. There were 37 patients operated upon after 4 days from the onset of symptoms, with 5 deaths, or a mortality rate of 13.5 per cent in this group. The over-all mortality rate was 8.2 per cent (table I).

The 5 patients who died ranged from 70 to 85 years of age. One of the patients (Mrs. W., age 76) who died had an acute cholecystitis with stones secondary to an adenocarcinoma primary in the gallbladder. She entered the hospital with an impending perforation. At operation a cholecystostomy and biopsy were done. She died 13 days postoperatively from her disease.

A second patient (Mrs. G., age 72) who did not survive had had recurrent attacks of gallbladder disease for nearly 30 years, and during the past year had had recurrent attacks of acute cholecystitis. Her last attack had occurred two months prior to her operation, and at that time she had been in the hospital for about

TABLE I

Time elapsed before surgery

Period of Time Elapsed after Onset of Symptoms before Surgery	Number of Patients	Number of deaths
Under 24 hours	7	0
24 to 48 hours	5	0
2 to 4 days	12	0
4 to 14 days	13	3
14 to 30 days	11	1
Over 30 days	13	1
Total	61	5

three weeks. She had in addition an acute pancreatitis with an amylase up to 368 at the onset, and subsequently she developed a cardiac decompensation. Postoperatively she did poorly. She developed an abscess in the lesser omental bursa, which was drained 3 weeks after the original operation. Subsequent to this she became afebrile, but her course continued down hill, and 5 weeks after the second operation she died of debilitation and cardiac failure.

The other 3 patients who failed to survive the operations were found to have free perforations at the time of operation. In all 3 a clinical diagnosis of perforation was made prior to the operation. One patient (Mrs. S., age 85), with a long history of gallbladder disease, was admitted to the hospital on the fourth day of her illness with an increasing jaundice. When seen in consultation on the following day she was showing improvement in her condition. Because of her advanced age, and improvement in the hospital during the previous 24 hours, conservatism was advised. However, 6 hours after the consultation she had a severe chill, the temperature rose to 106 F., and marked signs of perforation and peritonitis were evident. After preparation of several hours, because of initial shock, she was operated upon. A perforated gallbladder with a profuse peritonitis, and a huge common duct stone were found. Inasmuch as she weighed less than 90 pounds, it was possible to quickly remove the gallbladder, open the duct and remove the stone. She died on the fourth postoperative day.

The fourth to die was Mr. P., age 74, who was first seen in the hospital in consultation on the third day of his disease. Operation was advised as he had signs of imminent perforation, but he adamantly refused. On the following day rapid progression of the disease was noted with evidence of perforation, and he consented to operation. A perforated gallbladder with severe peritonitis was found. This patient proved to be allergic to all of the antibiotics, and eventually died of peritonitis and a superimposed pneumonia on the twentieth postoperative day.

The fifth death was Mrs. L., a 70 year old woman, who was transferred to one of our private hospitals from out of the city. At the time of admission she was intensely jaundiced and critically ill. She had been very ill for several days, with daily chills, temperature up to 104 F. or more, extremely high leukocytosis, and increasing signs of severe peritonitis. She was treated conservatively for almost a week by the medical service, but she continued to grow worse, and after overdue

consultation operation was decided upon literally as a last resort. At operation a perforated gallbladder, with severe peritonitis, and a huge stone in the common duct was found. She died two hours postoperatively.

In this series of 61 patients cholecystectomy was done in 59, cholecystostomy in 1, and in the other patient a perforation of an old stump of a previous partially removed gallbladder was removed and a choledocholithotomy was done. Choledocholithotomy was done in a total of 12 patients, 9 of whom were jaundiced.

SUMMARY AND CONCLUSIONS

A brief resume of acute cholecystitis with a discussion of the etiology, clinical features, differential diagnosis, and treatment has been presented.

The treatment of acute cholecystitis is elaborated upon, giving the arguments for and against early operation.

The danger signs in acute cholecystitis include: persistence of elevated temperature, tenderness and rigidity with or without a mass, severe pain without relief by morphine, increasing toxemia, rising leukocytosis, and a steadily rising pulse rate.

A clinical survey of 61 consecutive cases of acute cholecystitis is presented, with an over-all mortality rate of 8.2 per cent.

A plea is made for careful judgment in the treatment of these patients. We believe that the treatment for each patient should be individualized, and that by so doing the best results will be obtained. If seen nearly, at least before the fourth day after the onset of symptoms, early operation is the treatment of choice in our opinion. We do not believe that there should be any fixed time when operation should be contraindicated simply because of the element of time elapsed since the onset of the patients symptoms.

Prophylactic removal of all calculus gallbladders seen probably would eliminate a great majority of the cases of acute cholecystitis, and would thus greatly improve the mortality and morbidity statistics.

We favor cholecystectomy over cholecystostomy, but believe that the latter has a definite place in a few carefully selected patients. Choledocholithotomy may be done safely in the presence of acute cholecystitis in most patients.

The patient should always be adequately prepared for operation, with restoration of fluid balance, electrolytes and vitamins, and antibiotic therapy should be instituted prior to operation.

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SPONTANEOUS PERFORATION OF THE ESOPHAGUS WITH REPORT OF A CASE

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Spontaneous perforation of the esophagus can be considered a clinical entity with typical symptoms, signs, pathology and disturbed physiology. Almost invariably the patient is suddenly seized with severe substernal and lower chest pain simultaneous with or immediately following an episode of vomiting. The vomitus often is blood tinged or frankly bloody. This leads to a sequence of dyspnea, cyanosis, prostration and usually death within a few hours or days if the diagnosis is not quickly made so that surgical treatment can be instituted early.

Many reviews of this uncommon condition have been written and we will summarize some of the pertinent points in this report.[6, 14, 18, 23, 24, 25, 28, 39, 40, 44] Numerous case reports have been found.[2, 3, 4, 5, 7, 8, 10, 11, 13, 16, 19, 20, 21, 26, 27, 31, 35, 37, 41] It is evident that from the time Boerhaave described the first case in 1724[6] until 1946, when a patient was successfully treated by suture of the esophageal defect,[5] there was 100 per cent mortality in this condition.[25] In a recent article we note 53 cases reviewed, of whom 50 per cent of the patients survived.[14]

In the literature the following general points are elucidated: Distinction between spontaneous and traumatic or other types of perforation must be adhered to in discussing this subject so that other cases are not included in such a report.[23, 44] A triad[28] of vomiting, frequently of bloody material,[25, 44] severe lower thoracic pain and upper abdominal pain, and emphysema in the neck (50 per cent),[14] are most often mentioned. When rupture into the pleural cavity occurs early there is likely to be absence of emphysema in the neck.[44] Patients have sometimes indulged in heavy meals and some have indulged in alcohol immediately prior to perforation.[6, 23, 24, 28] However, these factors have been overemphasized in the past.[14]

Forty-four per cent of the patients have a history of peptic ulcer or indigestion of some type.[14] The most frequent error in diagnosis has been confusion with perforated peptic ulcer, resulting in exploration of the abdomen.[24, 25] Other diseases considered in the differential diagnosis have been coronary thrombosis, pancreatitis, mesenteric thrombosis, dissecting aneurysm, high intestinal obstruction or strangulation, diaphragmatic hernia, pneumothorax,[25] and pulmonary embolism.[18]

Perforation usually takes place into the left pleural cavity, sometimes into the right, and occasionally into both.[14] There is a preponderance of males to females 5 to 1. The age incidence shows that patients are usually over 40 years of age. No patient over the age of 70 has been reported to have survived this catastrophe.[14]

Treatment ideally consists of thoracotomy, closure of the perforation with

two rows of interrupted nonabsorbable sutures, followed by closed drainage of the mediastinum and pleural cavity.[38] In occasional cases not diagnosed early the patients have survived drainage of the pleural cavity, having temporary esophageal fistulas which have sometimes closed spontaneously.[2, 28]

CASE REPORT

The following case report presents a fairly typical picture of so-called spontaneous perforation of the esophagus.

R. E. B., a 72 year old white man, while working on a highway construction project as a flagman, had a sudden onset of severe chest pain and vomiting of bloody fluid while eating lunch by a roadside on Aug. 8, 1953. He quickly became unconscious and was transported to the emergency room of the Stormont-Vail Hospital, Topeka, Kansas, where he arrived at 11:30 a.m., about 30 minutes after the onset of the catastrophe. He was too ill to give a history. The history was obtained second or third hand from other workmen. In the emergency room he rallied enough to complain of severe chest pain and to request a semi-sitting position in order to relieve his labored respiration.

He was seen by an internist and a surgeon, who suspected that the severe pain, dyspnea, cyanosis, and profuse sweating were due to a coronary vascular accident or pulmonary embolus. The pulse was rapid and thready, the respirations were labored and 32 per minute, and there were rhonchi over both lung fields. There was slight tenderness in the right calf and popliteal space.

Fifty mg. of demerol apparently had little effect upon the pain. An electrocardiogram was of no diagnostic aid. The hemoglobin determination was 8 Gm. per 100 cc. or 52 per cent. Vomitus on the clothing was checked for blood and showed a positive benzidine test. While in the emergency room the patient had a black, involuntary stool, showing a three plus benzidine test. A chest roentgenogram showed pneumothorax around the left lung 2 cm. wide with minimal fluid at the base at that time.

At 1:00 p.m. I was asked to see the patient and take over his care because of the left pneumothorax. My first impression upon seeing him a few minutes later was that the severity of the symptoms and prostration were far out of proportion to the minimal hydropneumothorax that existed.

A left thoracentesis yielded about 250 cc. of air and 300 cc. of bloody, coffee-ground fluid, resembling the vomitus of a patient with a bleeding peptic ulcer. A small plastic catheter was inserted into the left pleural cavity at the time of the thoracentesis, and connected to a water seal suction bottle. The diagnosis of perforation of the esophagus into the left pleural cavity was made at that time.

The laboratory had difficulty obtaining satisfactory cross-matches for transfusions. While waiting, he was given 5 cc. of indigo carmine orally and further thoracentesis was done to try to recover the dye from the left pleural cavity. This was not conclusive. At thoracotomy the blue dye had produced a gray, muddy color when mixed with blood and gastric content.

Twenty cc. of lipiodol were given by mouth and portable semi-upright roentgenograms demonstrated a U-shaped pattern in the region of the lower esophagus, curving back up into the mediastinum with a less radiopaque air and fluid level adjacent to the shadow produced by the lipiodol. This was interpreted by the radiologists as a hiatal or parahiatal hernia with perforation of a viscus into the left pleural cavity. In retrospect, the U-shaped shadow was the pattern in which the lipiodol lay in the mediastinum and distended pulmonary ligament in this patient in a semi-recumbent position, and the fluid level was that typically seen in the widened mediastinum in perforation of the esophagus.[17, 24]

While the diagnostic procedures were being done the patient was having severe chills, increasing dyspnea, cyanosis, and persistent pain in spite of repeated doses of demerol. Continuous suction was applied to a Levine tube inserted into the stomach after the fistula had been demonstrated.

While the patient did not look as though he would tolerate operation, our supportive measures had little effect, and his general condition was rapidly deteriorating in spite of continuous oxygen administration since admission and blood transfusions.

The left chest was opened through the bed of the resected eighth rib at 7:15 p.m., approximately 8 hours after the onset of symptoms. At this time the blood pressure was 60/30, the pulse rapid, thready, and weak, with a rate of 120. The left pleural cavity contained approximately 1,000 cc. of dark, gastric content at this time, with many corn and pea shells. There was a perforation in the pulmonary ligament 1.5 cm. in diameter. The distended mediastinal pleura was opened widely and corn and peas were found extending above the hilar level. When the thoracic esophagus was mobilized, a longitudinal perforation 2.5 cm. in length and about 1.5 cm. in width was seen in the lower esophagus 5 cm. above a normal hiatus.

While no ulceration of the esophageal mucosa was detected, there was marked edema of the lower 5 cm. of the esophagus to the extent that other lesion was suspected. It did not appear that a two-layer closure of this rent would leave a functional lumen, and suture in a pathologic area was feared.

The patient's general condition had improved considerably after removing the gastric content from the mediastinum and pleural space. Therefore, the lower 7.5 cm. of esophagus were resected, after the diaphragm was opened, and the fundus of the stomach was delivered into the lower chest for esophagogastric anastomosis. The stomach was sutured to the mediastinal structures and partially closed diaphragm. The pleural cavity was drained with a large mushroom catheter in the tenth interspace with its tip near the mediastinum.

When the patient was moved from the operating table to his bed, he was awake. The blood pressure was 95/50, the pulse rate was 110 with fair pulse volume. He had received 6 pints of blood from the time of admission to the end of the procedure. There was minimal blood loss during the operation. Large doses of penicillin and streptomycin were administered.

His condition remained fairly good through the night with the blood pressure ranging from 95 to 108 systolic. On the following morning the hemoglobin was 14 Gm. per 100 cc. or 91 per cent, and the hematocrit level was 45. He was still receiving intravenous fluids and the urine output was satisfactory. During the morning there were several transient periods of cyanosis of brief duration, and the blood pressure fell to 84/62, with pulse rate 96 on one of these occasions. Due to his age and behavior we suspected inadequate adrenal response. One-hundred mg. of cortisone were given hypodermically at 9:15 a.m. At 11:00 a.m. the pulse volume was considerably improved. However, at noon the respirations became more labored, the pulse rate dropped to 56 and the blood pressure to 64/44. At 12:20 the patient died. We were unable to obtain an autopsy.

The microscopic pathology report of the resected esophageal segment was: "Reveals masses of muscle covered by stratified squamous nonkeratinizing epithelium. There are numerous dilated blood vessels, some of which are rather thin walled. There is some polymorphonuclear infiltration, marked edema, and some lymphocytic infiltration and apparent areas of necrosis. Diagnosis: Acute esophagitis, with apparent thrombosis of some major vessels."

It is now believed that most of the gross and microscopic changes in the esophagus occurred during the time between perforation and resection, but it does seem that some acute inflammatory process preceded the rupture.

DISCUSSION

This case illustrates many important features of spontaneous or postemetic[40] perforation of the esophagus.

While case reports suggest that vomiting always precedes perforation, a few state that pain preceded vomiting.[8, 20, 31, 34] Many of these patients such as ours are too ill to give an accurate history.

Experimental studies have shown that increased pressure in the esophagus is prone to produce rupture, usually in the lower one-third.[12, 15, 24, 29, 32, 46] It has been said that this usually occurs in a previously normal esophagus,[6, 41] and this view might be substantiated by reports showing rupture in the lower one-third as a result of accidental blows to the abdomen in both adults and children, in which only the mechanical factor of increased pressure would be functioning.[1, 14, 22, 33]

Some have contended that the catastrophe usually is accompanied by some pathologic process in the esophagus.[42] Recent experimental work upon dogs brilliantly demonstrates the relation of acid peptic esophagitis to perforation in that animal.[9]

A report of spontaneous perforation of the esophagus in only 1 patient, who had previously had an 80 per cent gastrectomy for peptic ulcer, would not clinically follow the acid peptic theory.[30] However, it is known that hydrochloric acid is not always essential to the production of lower esophagitis.[43]

Several reports state that the patient's own impression was that he was having an acute illness or the "*flu*" preceding or at the onset of the vomiting.[18, 20, 21, 41] An acute process in the esophagus similar to acute regional enteritis occurring in the terminal ileum is not inconceivable.

In reading over case reports it is interesting to note that several perforations of the esophagus occurred in patients hospitalized for other serious disturbances or for routine surgical operations.[4, 5, 20] Several factors during surgical operations and in the postoperative period have been shown to contribute to lower esophageal ulceration, or it may be that the patients' residence in the hospital at the time of perforation contributed to accurate diagnosis in these particular cases making the incidence less significant.

In retrospect, delay in thoracotomy, in spite of low hemoglobin and extreme prostration, was not justified in this case. The condition deteriorated although the patient was given blood transfusions and continuous oxygen therapy. This has been emphasized previously.[13, 18, 25]

A patient's condition often improves as the gastric contamination is irrigated from the pleural and mediastinal spaces.[5, 21, 26] However, it is also noted that some relapse 12 to 36 hours postoperatively.[8, 13, 21, 25] There is no question but that lower esophageal perforation with escape of gastric content into the mediastinum and pleural cavities is more grave with a much worse prognosis, in spite of surgical treatment, than perforation of a peptic ulcer into the abdominal cavity.

There is little argument in favor of any treatment of spontaneous or postemetic esophageal perforation other than early definitive thoracotomy with closure of the defect and closed drainage of the pleura and mediastinum.[25, 36, 38] For the most part, early direct surgical closure of any esophageal fistula is advocated in this country.[36, 38, 45]

It is interesting to note that Karcher in Germany reported a 100 per cent survival rate after conservative therapy in 9 post-traumatic perforations, and advocated no more treatment than antibiotics, aspiration and rib resection if necessary.[22] Such perforations diagnosed in a hospital after a procedure that

commonly produces a rent in the esophagus or when a foreign body is involved, where perforation may be expected and is looked for, cannot compare with the spontaneous perforation accompanying the emetic force which projects large quantities of gastric content into the mediastinum and pleural cavity. Recently there has been an account of almost 100 per cent survival rate of patients with traumatic and instrumental rupture of the esophagus treated by closure of the esophagus,[45] in contrast to 50 per cent survival rate in spontaneous perforation of the esophagus.[14] It is expected that with earlier diagnosis and more aggressive definitive treatment the percentage of survivors in spontaneous perforation will continue to rise.

CONCLUSIONS

Spontaneous or postemetic perforation of the esophagus is a clinical entity which can be easily diagnosed on the basis of the history, physical findings, and laboratory procedures which are available in any hospital. It is important that the diagnosis be suspected and made with dispatch so that open thoracotomy with closure of the esophageal wound, followed by closed drainage of the mediastinum and pleural cavity, will be effected without delay.

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DELAYED HEMOTHORAX DUE TO TRAUMATIC RUPTURE OF THE INTERNAL MAMMARY ARTERY: A CASE REPORT*

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Massive hemothorax is an uncommon result of thoracic injury. The diagnosis in such a case usually offers little difficulty, and the management is now fairly well defined and agreed upon. The following case is reported because of two unusual features, viz., a 12 hour delay in the onset of major bleeding, and the rupture of a major chest wall artery without associated rib or sternal fracture. A search of the recent literature failed to disclose any report of a similar case of hemorrhage from the internal mammary artery.

CASE REPORT

The patient was a 33 year old, Negro man packing house worker. At about 5:30 a.m. on the day of admission, a car which he was driving struck a utility pole and he was thrown hard against the steering wheel striking his lower chest and epigastrium. He was somewhat dazed but walked away from the accident to summon help. He noticed some chest pain and some bleeding from a cut on his lip. He was brought to the hospital about 8:30 a.m. mainly because of his cut lip. On admission, he complained of increasing retrosternal and left chest pain, left shoulder pain, and some shortness of breath. He had not had any cough or hemoptysis.

Physical examination on admission showed a well developed, well nourished, Negro man who was in acute distress. His oral temperature was 97.4F. His blood pressure was 130/80. His pulse was regular and its rate was 100 per minute. A small cut on his upper lip was bleeding slightly. Neurologic examination did not show any abnormality. The patient maintained a hunched forward posture and groaned with each inspiration. His respirations were shallow and rapid but his chest moved symmetrically. No external abrasions or contusions were visible on his thorax. However, his entire anterior chest, especially over the sternum and the left lower ribs, was exquisitely tender to palpation. Lateral compression of his chest produced no point of pain indicative of rib fracture. The percussion note and breath sounds were normal throughout both lung fields. The cardiac area of dullness and sounds were normal. Some epigastric tenderness and mild abdominal distension were present. The remainder of the examination was essentially negative.

Laboratory findings on admission. The red blood cells were 4.20 million per cu. mm., hemoglobin 12.5 grams per 100 cc., white blood cells 10,000 per cu. mm., and hematocrit level 40 per cent. A roentgenogram of the chest on admission was essentially normal. No evidence of rib fractures, hemothorax, or pneumothorax was present.

Initial impressions were: (1) Contusion and laceration of the upper lip, (2) contusion of the chest wall, and (3) possible rib fractures and/or minor pneumothorax.

The patient was admitted for observation even though his injury appeared to be minimal. He did well during the day except for chest pain which was controlled with acetylsalicylate compound and codeine. He took a full liquid diet well and walked to the examining room to be re-examined in the late afternoon. At 6:10 p.m., slightly more than 12 hours after the accident, he suddenly became quite dyspneic, and his respirations increased to 40 per minute. His pulse became weak and its rate rose to 120 per minute. His blood pressure

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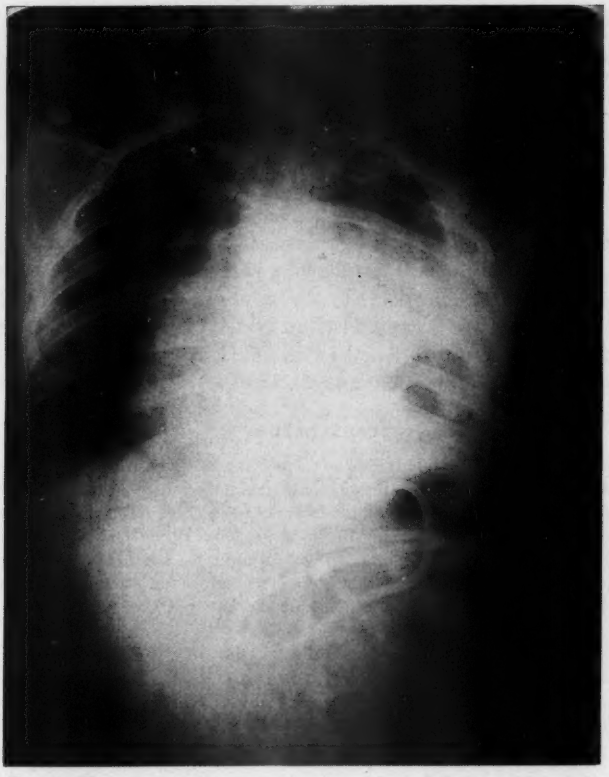

FIG. 1. Chest roentgenogram after insertion of thoracostomy tube

fell to 85/60. His skin became cold and clammy. Nasal catheter oxygen was started at once and 1000 ml. of dextran solution was rapidly infused while blood typing and crossmatching were being done. Physical examination then showed dullness throughout the left hemithorax and a shift of the trachea toward the right. Thoracentesis produced bright red blood in quantity. A closed thoracostomy was done using a no. 18 F soft rubber catheter in the eighth interspace with a dependent water seal. In a very few minutes, 1000 ml. of blood was collected from the thorax. A portable roentgenogram made at this time (fig. 1) confirmed the diagnosis of massive left hemothorax. By this time compatible blood was available in quantity and transfusions were begun. The pulse became stable at about 120 per minute and the blood pressure rose to 140/80. Breath sounds reappeared in the left lung field. Over the next three hours, bleeding continued from the chest at a rate of about 500 ml. each 30 minutes and a corresponding quantity was given by transfusion. Despite this, the patient's pulse rate gradually increased to 140 and his blood pressure fell to 104/60. Thoracotomy was done at 11:30 p.m., five hours after the onset of bleeding. The thorax was entered through the left fifth interspace. About 500 to 600 ml. of blood clot and an equal quantity of fresh blood were removed. Active bleeding was found from the left internal mammary artery which had been disrupted at the level of the fifth rib. This was ligated with no. 00 black silk. The areolar tissues of the mediastinum were suffused with blood. Hemorrhage had dissected the anterior mediastinum from the posterior surface of the sternum. There

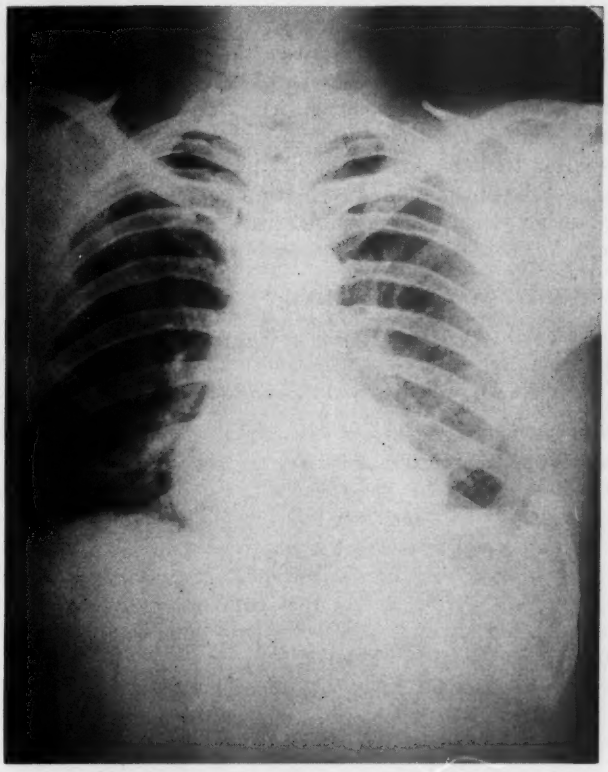

FIG. 2. Chest roentgenogram at time of discharge

was a large rent in the parietal pleura where it is reflected off the anterior chest wall onto the mediastinum. A minimal oozing from the posterior aspect of the sternum was the only other bleeding encountered. No rib or cartilaginous fractures were noted and no injury to the lung or the pericardial or mediastinal organs was found. The mediastinal tear was loosely closed with no. 00 black silk, all blood was removed from the chest cavity, and the thoracic wall was closed leaving low posterior and high anterior drainage tubes in the chest. These were attached to dependent water seals. His postoperative course was entirely uneventful. No further bleeding occurred and his pulse and blood pressure remained normal. His lung rapidly expanded and remained so and his drainage tubes were removed after 48 hours. His wounds healed per primam. He was sent home on his eleventh postoperative day. A chest roentgenogram made on the day of discharge showed minimal pleural thickening in the left lower lung field, but otherwise was essentially normal (fig. 2). He was symptom free.

COMMENT

A possible sequence of events is the following. The left internal mammary artery was ruptured at the time of the injury. This produced a slowly dissecting hematoma which caused persistent severe substernal pain. The tissue pressure at

first prevented exsanguinating hemorrhage, but, when rupture into the left pleural cavity occurred, massive hemorrhage and shock followed.

Rupture of a major chest wall vessel without concomitant fracture of the thoracic cage is exceedingly uncommon. The delayed development of major shock-producing hemothorax also is quite rare. Most patients who develop hemothorax after trauma have diagnostic physical signs and/or roentgenographic findings when they are first seen at a hospital shortly after their injury. Seldom does such a patient have a normal chest roentgenogram on admission as did this one.

SUMMARY

A case of delayed post-traumatic hemothorax resulting from rupture of the left internal mammary artery without concomitant thoracic cage fracture is presented. Complete recovery followed thoracotomy and ligation of the artery.

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SURGICAL TECHNIC

REPAIR OF SURGICAL DEFECTS OF THE CHEST WALL WITH FIBERGLAS PROSTHESIS*

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Reconstructive methods for defects of the chest wall encompass fundamental problems of primary wound closure and maintenance of stability, the latter depending upon the location and magnitude of the defect. The use of bone,[3,7,8] periosteal flaps,[9] and fascia lata strips[11] are limited to small defects. Thoracoplasty with collapse of the chest wall imposes the serious consequence of decreased ventilatory function. In large defects of the anterior and lateral aspects of the chest wall, stability must be secured to prevent the deleterious effects of paradoxical respiration, abnormal mediastinal mobility, and inability of the patient to produce a forceful cough in the immediate postoperative period. The use of external appliances to provide support for large chest wall defects has proved unsatisfactory. Metal prosthesis seriously limit roentgenologic examination of the underlying lung parenchyma.[1, 2, 4, 12] The practicability of preformed lucite plates for the reconstruction of major chest wall defects has been recently reported by us.[5] Lucite plates are suitable for providing stability to the chest wall, are satisfactorily tolerated by the body tissues, and permit primary wound closure. These plates are radiolucent. Lucite does have the slight disadvantage of requiring preoperative cutting, shaping, drilling of holes for suturing, and of cold sterilization. Because of these disadvantages of lucite we were attracted by the possibilities of Fiber glass as a prosthesis for large chest wall defects.

Fiberglas† cloth is woven from inorganic glass yarns. It can be obtained in a wide range of specifications, according to the size of the fiber. This fabric does not absorb moisture and is insoluble in organic solvents. It is easily sterilized by autoclaving. The cloth can be readily fashioned to the size of the defect.

O'Neil and associates[10] utilized Fiberglas fabric to invest selected lobes of the lung for segmental atelectasis. In both experimental and clinical trials the tissue reaction was minimal. Upon removal of the Fiberglas fabric the lungs were able to expand completely to their normal positions.

Fiberglas cloth has been used by us in the repair of large abdominal and inguinal hernial defects with satisfactory results.[6]

The following experimental procedures were done to repair surgically created defects of the chest wall utilizing Fiberglas cloth.

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† Fiberglas is the trade name of Owens-Corning Fiberglas Corporation, Toledo, Ohio.

EXPERIMENTAL METHOD

Ten mongrel dogs were operated upon under endotracheal positive pressure anesthesia. Surgically created defects were made in the anterolateral thoracic wall measuring 10 by 10 cm. The skin and subcutaneous tissue was preserved for primary closure over the prosthesis. The surgical defects were covered with autoclaved Fiberglas cloth (Type 119). On cutting of this material the ends tend to fray. Prior to fixation of the prosthesis into the defect the edges of the cloth were folded and fixed with a continuous locking no. 000 silk suture to prevent this fraying and to give additional points of fixation to the thoracic wall. The patterned Fiberglas prosthesis then was sutured into the defect with interrupted no. 30 stainless steel wire. Stability of the chest wall was obtained by the inserted prosthesis. The subcutaneous tissue and skin then were closed in layers over the cloth. A colloidion dressing sealed the thoracic incision and negative intrathoracic pressure was applied. Penicillin was given postoperatively for 10 days. All of the 10 animals survived the operative procedure and were killed at monthly intervals up to 9 months.

There was no evidence of postoperative hernia or infection in any of the animals. Tissue tolerance was excellent without any tendency to extrude the prosthesis. The repaired areas were strong and stable. The incisional scar moved freely over the prosthetic cloth. Microscopic sections showed a firm fibroelastic infiltration around and into the cloth. Minimal adhesions were present between the lung and Fiberglas.

CASE REPORTS

The following clinical cases illustrate the problems in radical resection of the chest wall and the application of Fiberglas in their resolution.

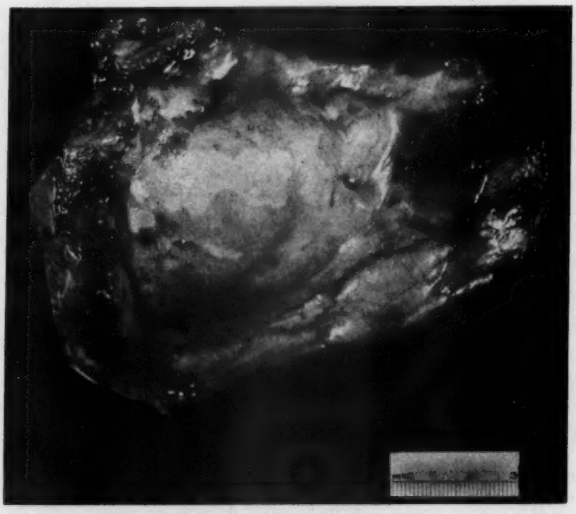

FIG. 1. Surgical specimen of neurofibrosarcoma of chest wall

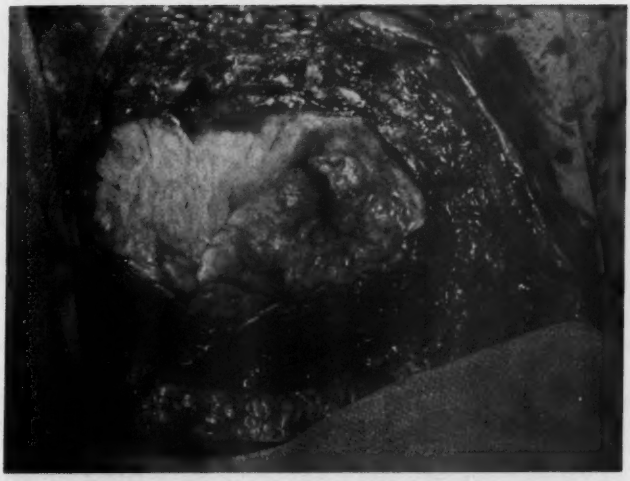

FIG. 2. Defect of thoracic cage overlying chest wall tissues preserved for coverage

Case 1. M. S., a 32 year old white woman was admitted to the University of Kansas Medical Center on April 17, 1951. Onset of symptoms began five years ago with pain radiating along the right anterior sixth rib. A roentgenogram taken at that time was interpreted as showing costochondral separation. She had her chest taped and received symptomatic relief. There was recurrence of the pain in the same location intermittently every two or three months. During pregnancy in 1948 she was unable to nurse her child because of pain over the right anterior chest wall. One month prior to admission a roentgenogram showed

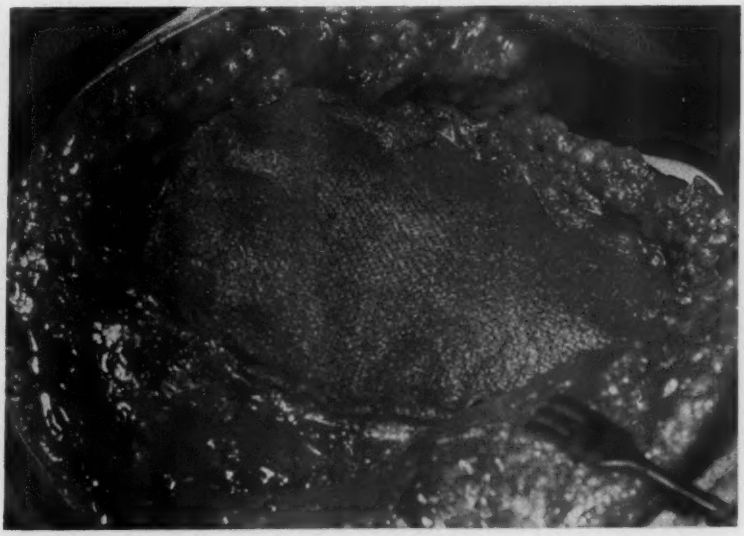

FIG. 3. Repair of defect with Fiberglas prosthesis

rib destruction of the sixth and seventh ribs anteriorly in the midclavicular line. On physical examination there was a tender mass measuring 3 by 5 cm. fixed to the sixth and seventh ribs below the breast fold in the midclavicular line. Roentgenograms of the chest showed no parenchymal spread of the tumor.

On April 18, a thoracotomy was done with resection of the right fifth, sixth, and seventh ribs en bloc including the medial ends of the costal cartilages (fig. 1). In the tendinous portion of the diaphragm there were numerous hard firm nodules which were resected. A 7 by 7 cm. defect in the diaphragm was reconstructed by means of continuous chromic catgut sutures. One similar nodule was resected in the area of the pulmonary ligament. The resultant defect in the anterior chest wall measured 10 by 15 cm. and this was closed by means of a double layer of Fiberglass cloth (figs. 2, 3). The pathologic diagnosis was neurofibrosarcoma. This patient required four thoracenteses during her first 10 days postoperative period, the total quantity of fluid removed being 1600 cc.

Comment: Since this tumor was completely contained within the thoracic wall the overlying soft tissues and skin were used for coverage of the Fiberglas cloth. A rigid, supple, painless chest was noted on follow-up (fig. 4). The overlying tissues moved freely over the prosthesis. The patient died two and one-half years

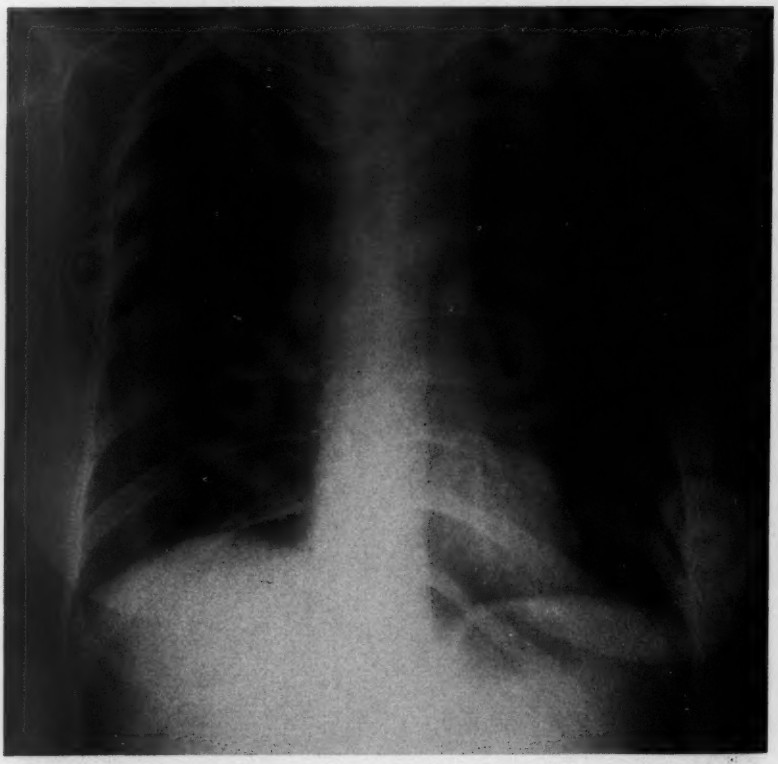

FIG. 4. Roentgenograms of chest two years after operations showing underlying lung parenchyma.

following operation from generalized metastases. The operative sites were free of tumor.

Case 2. O. F., a 67 year old woman was admitted to the University of Kansas Medical Center on July 2, 1951. Two months prior to admission she noticed a growth on the right posterolateral aspect of the chest wall situated well below the inferior angle of the scapula. She also complained of a cough for the past two weeks, which was productive, but without hemoptysis. There was persistent pain and soreness localized to the same area requiring narcotics for relief. An 8 pound weight loss was noticed during the previous two months.

On physical examination a 7 by 7 cm. firm mass was present at the level of the fourth right thoracic vertebra in the posterolateral aspect of the chest wall. In addition there was almost complete opacity of the entire right lung field interpreted as an underlying tumor shadow. The patient had generalized arteriosclerosis with arteriosclerotic heart disease. Bronchoscopy showed tracheal deviation to the left with no tumor visualized in the bronchial tree suggesting an extrinsic mass.

On July 23, a thoracotomy was performed. Exploration of the chest done through the bed of the fifth rib showed a large tumor mass occupying almost the entire posterior right upper lobe. This tumor mass was adherent to the chest wall over the sixth, seventh, eighth, and ninth ribs of the posterolateral aspect of the chest wall. Extensive metastatic spread of the tumor was noticed along the course of the superior vena cava, into the pulmonary hilum, and over the pericardium. Because of this extensive involvement, resection was not deemed advisable. However, because of the localized pain in the chest wall, palliative resection of the sixth, seventh, eighth, and ninth ribs was done. This block of tissue included skin, ribs and pleura. The resultant defect of the body wall measured 12.5 by 12.5 by 10 cm. This defect was closed with Fiberglass cloth. Soft tissue coverage was readily accomplished by shifting adjacent muscle groups with primary skin closure. Catheter drainage was instituted through the fourth and ninth interspaces anteriorly. The pathologic diagnosis was anaplastic carcinoma of the lung. The patient's postoperative course was uneventful. No thoracenteses were required.

Comment: Although the generalized spread of carcinoma throughout the vital structures of the chest cavity made pneumonectomy inadvisable, this patient obtained a great deal of palliation from the removal of the metastatic mass in her chest wall. Postoperatively she was more comfortable and at the time of discharge did not require the use of narcotics. A stable, rigid reconstructed chest wall was readily fashioned by means of Fiberglas. The patient died three months postoperatively.

Case 3. C. H., a 53 year old man was admitted to the University of Kansas Medical Center on Dec. 30, 1952. A United States Public Health Survey film of his chest in 1951 had disclosed a density in the right lower lung field. He was advised to have further medical consultation, but disregarded this recommendation. A repeat roentgenogram of his chest in 1952 showed that the lung lesion had increased in size. Simultaneously, he noted the onset of a painful hard mass in the upper right anterior chest wall accompanied by nonproductive cough for approximately nine months. Clinically the mass measured 13 cm. in diameter and was located just below the clavicle and extended from the lateral edge of the sternum to the midaxillary line. Chest roentgenograms at admission showed a laterally situated mass 10 cm. in diameter appearing to occupy the peripheral portion of the right middle lobe of the lung with almost complete destruction of the fourth rib. Biopsy established the diagnosis of chondrosarcoma.

On Jan. 12, 1953 a right thoracotomy was done with resection of the second, third and fourth ribs together with the tumor mass, the adjacent pectoral muscles and the overlying skin (fig. 5). The lateral portion of the middle lobe was excised. An elliptical surgical defect

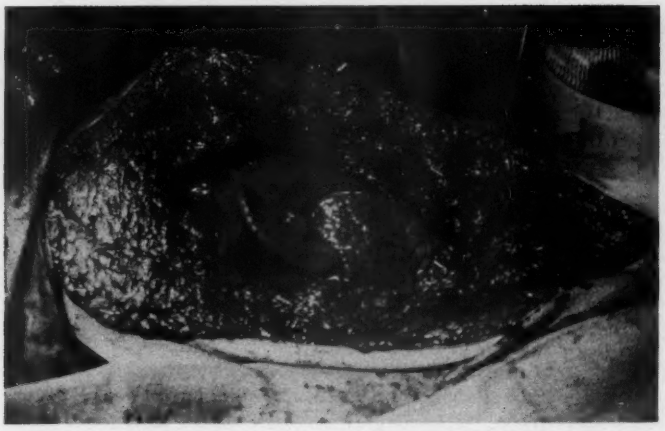

FIG. 5. Surgical defect of resected chest wall chondrosarcoma

of the thoracic wall resulted which measured 18 by 19 cm. Numerous metastatic nodules were noted along the posterior portion of the sternum, and the superior vena cava. The chest wall defect was closed with a double layer of Fiberglas (Type 108). Skin flaps were placed directly over this prosthesis with dependent drainage with rubber penrose tubes. Catheter suction was instituted to drain the pleural space. The patient's postoperative course was uneventful and thoracenteses were not required. He was discharged on January 31.

At the time of discharge there was approximately 4 to 5 cm. of movement in the reconstructed portion of his chest wall on forced respiration When seen in the outpatient clinic approximately one month after discharge the chest wall was quite firm and no motion was noted with straining or deep inspiration.

FIG. 6. Interscapulo-thoracic amputation with resection of anterior chest wall

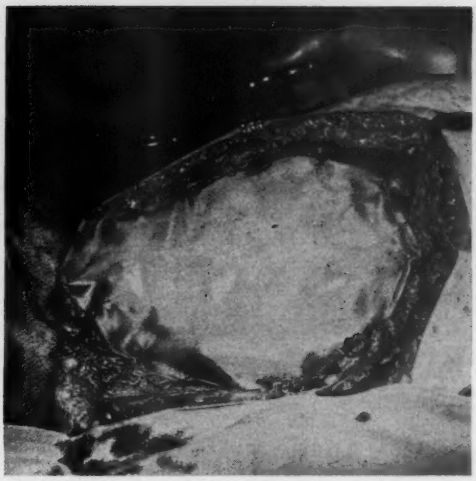

FIG. 7. Chest wall reconstructed with Fiberglas

Comment: This reconstructed defect healed per primum giving a stable chest wall with preservation of chest wall configuration, and minimal abnormality in ventilatory function. Four months later he developed cerebral metastases and died six months after operation.

Case 4. M. H., a 63 year old woman was admitted to the University of Kansas Medical Center on Feb. 9, 1953. Her symptoms began in 1945, with the development of a small

FIG. 8. Coverage of prosthesis with a skin flap developed from the lateral and inferior portion of the arm before amputation.

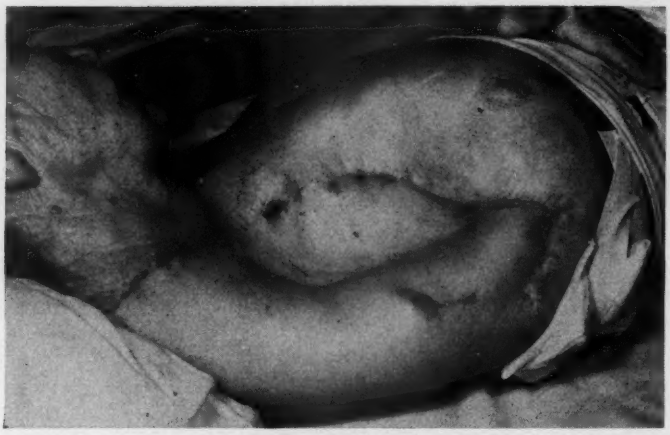

FIG. 9. Appearance of chest wall after Fiberglas prosthesis had to be removed because of infection.

subcutaneous nodule in the right upper arm. No biopsy was taken but she was given radiation therapy. During the next four years the tumor mass regressed slightly in size but never completely disappeared. In 1951 the skin over the anterior axillary fold became ulcerated.

Physical examination disclosed an 8 by 12 cm. tumor mass over the upper medial deltoid area. The axilla was extensively scarred and bound to the chest wall. The center of the tumor mass was ulcerated with a peripheral circumferential field of radiodermatitis. Roentgenograms of the chest with particular attention to the scapula and the humerus failed to show any abnormality. A biopsy showed fibrosarcoma.

On Feb. 12, 1953 an interscapulo-thoracic amputation with resection of the anterior portions of the first to fourth ribs was done (fig. 6). This resulted in a 12 by 14 cm. defect

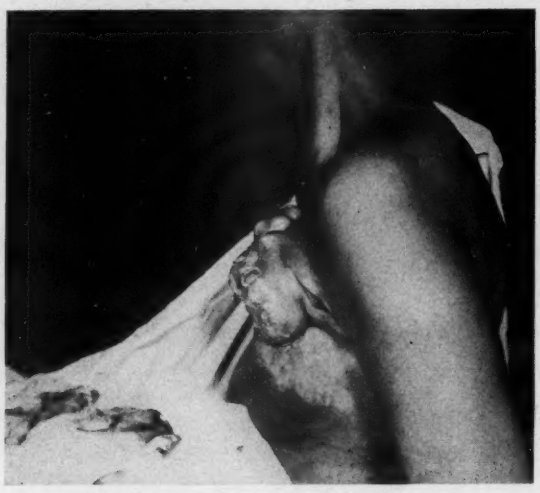

FIG. 10. Ulcerated fixed carcinoma of breast

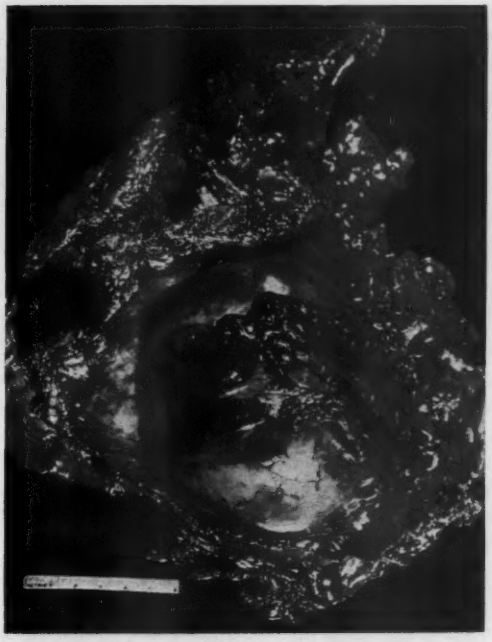

FIG. 11. Surgical specimen consisting of breast and chest wall

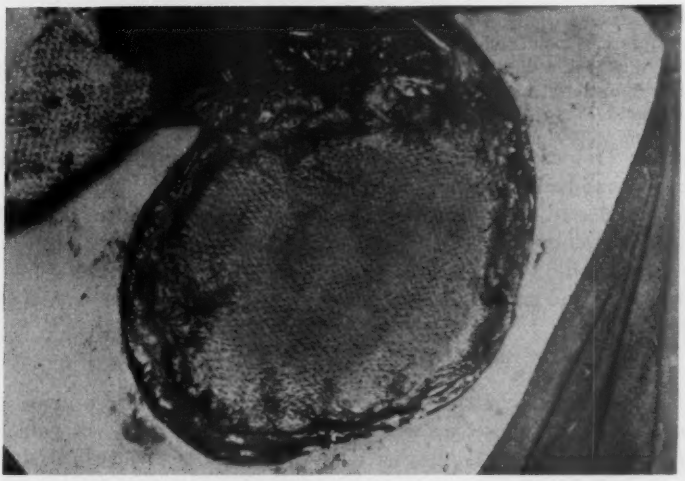

FIG. 12. Reconstructed chest wall with Fiberglas. The opposite breast was mobilized and rotated to cover the prosthesis.

in the chest wall. A layer of Fiberglass fabric (Type 127) was sutured to the edges of this oval defect (fig. 7). This prosthesis was covered with a skin flap developed from the lateral and inferior portion of the arm area (fig. 8). A catheter was inserted to drain the pleural cavity.

Her postoperative course was complicated by a febrile reaction with purulent drainage from beneath the skin flaps, noted 36 hours following operation. Culture showed a Proteus organism sensitive to Chloromycetin. Purulent material also was noted coming from the pleural cavity and culture of this showed the same organism. Numerous thoracenteses were done in an attempt to manage this empyema conservatively. On February 29, the Fiberglass prosthesis was removed and the lung decorticated. Following this procedure her recovery was uneventful.

Comment: This tumor apparently was malignant from onset but grew slowly during the many years before its radical resection. The infection incurred postoperatively may well have resulted from decreased tissue vitality secondary to the extensive radiation therapy. In the presence of this infection the Fiberglas acted as a foreign body and had to be removed. Whenever primary soft tissue wound closure cannot be done the prosthesis must be covered by a direct, rotated, or sliding flap of normal adjacent tissue. The removal of the prosthesis necessitated by infection destroyed a pleasing configuration of the right shoulder and collapsed the underlying lung tissue (fig. 9). At the time of this report (Sept. 15, 1955) the patient is free of any evidence of recurrence.

Case 5. R. P., a 71 year old Negro woman, entered the University of Kansas Medical Center in October of 1953. A left breast mass was first noted in 1950. She had received no treatment. At the time of admission the left breast was ulcerated and fixed to the chest wall. The mass of tumor measured 16 by 14 cm. The underlying fourth rib showed destruction by the tumor (fig. 10). A chest roentgenogram was negative for intrathoracic extension of the tumor. She was operated upon Oct. 18, 1953 at which time a radical mastectomy was done with a resection of the chest wall from the second to fifth ribs. (fig. 11). The resultant chest wall defect was closed with Fiberglass (Type 119). To provide soft tissue coverage the right breast was mobilized upward and placed over the prosthesis (fig. 12). The denuded area below the mobilized breast was covered with split-thickness skin grafts. The pleural cavity was drained with a catheter. The pathologic diagnosis was ulcerating carcinoma of the breast.

Comment: This patient died seven days postoperatively from a pulmonary embolus. No residual tumor was found at the operative site. Resection in continuity was selected because of bony wall involvement. Local recurrent breast cancer may spread by direct extension or local lymphatic emboli with any generalized systemic spread.[12] Upper inner quadrant recurrence also lends itself to intrathoracic spread and simultaneous internal mammary dissection can be done at the same time.

SUMMARY

Radical resection of chest wall tumors should be restricted to primary lesions with or without contiguous metastasis. It is doubtful if sufficient palliation is obtained from the removal of other chest wall tumors to justify such an extensive procedure.

The utilization of a Fiberglas prosthesis preserves a stable postoperative chest

wall and minimizes the complications of abnormal mediastinal mobility. Fiberglas can be prepared by routine autoclaving, cut to any size at the time of operation, and readily fitted to a chest wall defect. Postoperative roentgenologic visualization of the underlying lung parenchyma is possible because Fiberglas is radiolucent. It is well tolerated by adjacent tissues.

The problems of reconstructing massive chest wall defects are illustrated by suitable case reports.

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A TECHNIC OF WOUND CLOSURE FOLLOWING RADICAL MASTECTOMY

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Since Halsted[1] first described the now classic radical mastectomy, the problem of collection of serosanguinous fluid under the skin flaps has always existed. Such an accumulation of fluid predisposes to wound infection, delay in healing, excessive scar tissue formation, and possibly increased postoperative edema of the arm.

A technic of wound closure is here presented which it is believed minimizes exudate collection and hence its complications.

Following removal of the breast by an S-shaped incision (fig. 2) which has been described previously,[4] the entire wound area is irrigated with warm physiologic saline solution. After careful hemostasis is assured the latissimus dorsi and subscapularis muscles are sutured to the intercostal muscles to reduce dead space (fig. 1). Tension sutures of heavy silk or cotton (no. 00) are placed through the skin flaps parallel to the edge of the incision and about 4 to 6 centimeters from this edge (fig. 2). As the drawing indicates, these are tied over rubber tubes, and the ends left long. When these are in place, the skin may be approximated with almost no tension on the suture line. A penrose drain then is placed in the axilla and brought through the skin a few centimeters below the lateral terminus of the wound. Using this same type suture as coaptation sutures, the superior skin flap is carefully sutured down over the axillary vessels and brachial plexus to the intercostal muscles. Sutures also hold the skin in contact with the coracobrachialis muscle, the short head of the biceps, the lateral stump of the pectoralis major, and to the latissimus dorsi muscles. All these sutures are placed to obliterate subcutaneous dead space, the existence of which is inevitably followed by accumulation of fluid exudate.

The long ends of these sutures then are utilized to retain in position a pressure dressing of mechanic's waste (fig. 3). An outer covering of elastic bandage completes the protection of the wound.

DISCUSSION AND SUMMARY

The principle of suturing the skin flaps to the chest wall and folding the skin high into the axilla is not new.

Halsted,[2] in 1913, advocated suturing the axillary skin to the intercostal muscles beneath the axillary vessels with buried sutures of fine silk. A similar procedure, using a basting mattress suture, was described by Keyes, Hawk, and Sherwin[3] in 1953.

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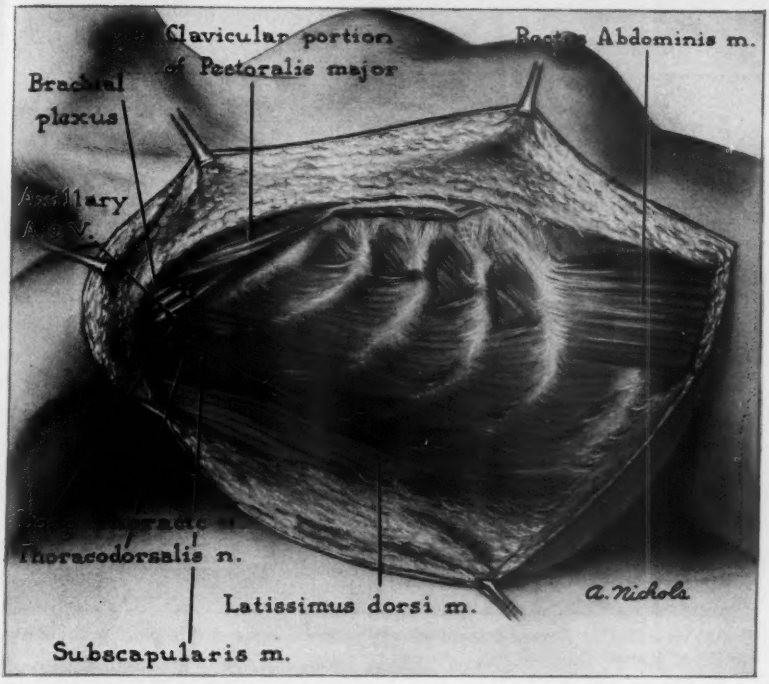

FIG. 1. Appearance of wound after removal of breast showing anatomic landmarks. The latissimus dorsi and subscapular muscles have been sutured to the intercostal muscles to obliterate dead space.

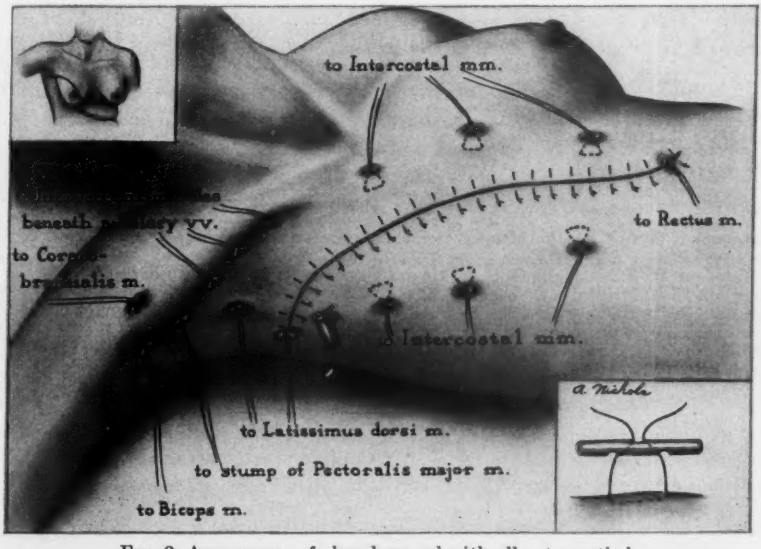

FIG. 2. Appearance of closed wound with all sutures tied

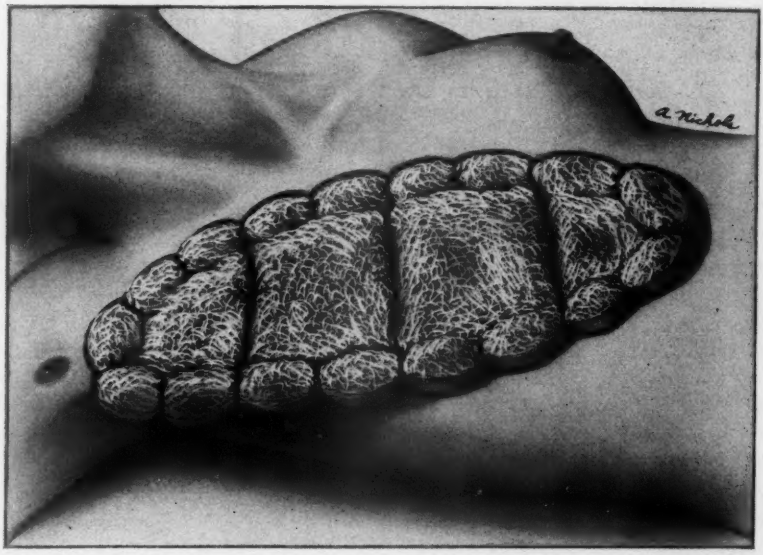

FIG. 3. Wound after closure dressed with mechanic's waste tied in place with long ends of tension and coaptation sutures.

The advantages to be emphasized in the method of closure here presented are: (a), obliteration as well as possible of all subcutaneous dead space, (b), immobilization of skin flaps against the chest wall and soft tissue, and (c), prevention of excessive tension on the skin suture line. Small areas of cutaneous pressure necrosis may occur at the sites of the tension sutures, which will heal promptly following stitch removal.

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TRANSABDOMINAL COLOSCOPY*

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Endoscopic examination and treatment of polyps of the rectum and lower sigmoid colon are well established and standardized procedures. Polypoid lesions of the remainder of the colon are of the same significance as those in the sigmoid and rectum, but because of poorer accessibility their diagnosis and treatment presents a somewhat more difficult problem. The diagnosis of such lesions above the level which can be visualized through the sigmoidoscope rests entirely upon roentgenologic examination either by barium enema or air contrast studies, and the difficulties in visualizing such polyps are well known. Under ideal circumstances current radiologic methods are probably not more than 50 per cent accurate in identifying such lesions.[2] Likewise, polyps clearly demonstrated by roentgenogram may prove difficult to identify at operation either because of their small size or due to their attachment by a long pedicle upon which they may move up or down the colon. This is especially true in an obese patient.

Because of this difficulty in identifying lesions through the intact colon at operation, although previously identified by roentgenogram, as well as a suspicion that many polyps are missed by the roentgenogram, it has been our practice for the past several years to do routine endoscopic examination of the entire colon through a sterile sigmoidoscope at the time of exploratory operation. This procedure has proved most satisfactory in that many polyps not seen on the roentgenogram have been found by coloscopy at operation. The hazards of contamination are minimal with good bowel preparation and careful precautions to avoid soilage. This technic also should be helpful in cases of colonic bleeding for which no cause can be found by using the usual diagnostic methods.

No claim is made for originality since this procedure is used elsewhere; however, none of the standard textbooks of surgery or of diseases of the colon refer to this technic for routine handling of colon polyps.

TECHNIC

Preoperative preparation is the same as for any major colon surgery. This thorough preparation is essential to avoid postoperative complications due to spillage of colonic contents into the peritoneal cavity or into the wound. We have used one of the insoluble sulfonamides for five days, usually adding neomycin for 24 hours prior to operation, although good mechanical cleansing of the bowel is in our opinion the most important preparatory measure. A long intestinal decompression tube also is passed on the day before operation. This not only contributes to more satisfactory cleansing of the colon but also simplifies the operative procedure by eliminating any distended loops of small bowel which

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might be troublesome. This tube is left in place following operation until active peristalsis returns.

We have found a left paramedian incision to be satisfactory for obtaining optimum exposure, although a transverse incision may be equally satisfactory.

Following manual examination of the abdominal contents, the sites of colotomy are chosen. These will vary somewhat depending on the preoperative roentgenograms, as well as individual variation in the length and degree of mobility of the colon. Any standard sigmoidoscope which can be sterilized is suitable. We have found distal lighting to be more satisfactory than proximal lighting. In addition a long suction tip as well as a long insulated fulgurating tip and fulgurating snare should be included in the set. This set-up is kept sterile in our operating room at all times and may be useful in examining the stomach or bowel in patients who are bleeding when the site cannot be determined from external examination at laparotomy. In many instances the entire colon can be examined through two colotomies, one at the junction of the descending and sigmoid colons and a second in the transverse colon usually slightly to the left of the midportion. The rectum and lower sigmoid will have been examined preoperatively by sigmoidoscopy. In one patient it was possible to pass the sigmoidoscope from a transverse colotomy through the ileocecal valve into the terminal ileum. One, or rarely two additional openings may be necessary when the colon is long or when mobility is slight. When the site for colotomy has been chosen and the remainder of the peritoneal cavity packed off with moist tapes, a small linear opening is made on the antimesenteric border of the colon usually through a taenia. Tight control to prevent spillage of colon contents or air introduced through the sigmoidoscope can be obtained by placing a purse string suture

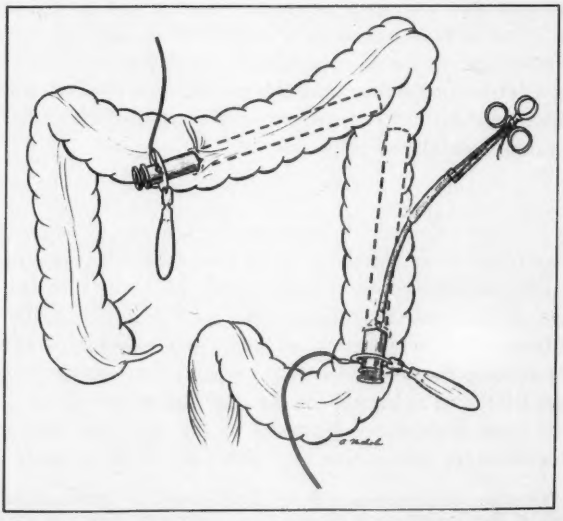

FIG. 1. Drawing showing the sites of colotomy through which the entire colon can be visualized in most instances.

about the opening and controlling it with a Rumel vascular tourniquet as depicted in figure 1. Careful examination of the colonic mucosa then can be made in both directions. Any lesions visualized then can be treated by fulguration, excision or segmental resection as indicated. The openings in the colon then are closed as preferred by the individual operator.

DISCUSSION

There is some question about how these lesions should be handled once they have been visualized, and a detailed discussion is not within the scope of this paper. However, the development of carcinoma from polypoid lesions of the colon is a well accepted fact.[1] In general it has been our policy to do segmental resection of the bowel for sessile polyps over one-half centimeter in diameter or for short, thick pedunculated polyps. Frozen section of tissue from a polyp, although of questionable reliability, may be of value in doubtful cases.[3] Resection is also done when multiple polyps involving a short segment of colon with few polyps elsewhere are found. Other lesions are removed by fulguration. It should be emphasized that great caution must be practiced when employing the electrocautery since tissue necrosis may be produced for a considerable distance beyond the point of contact. When this occurs late perforation may result. There is less danger of distal tissue necrosis when a low intensity current is employed.

The necessity for careful and systematic follow-up studies on all patients with colon polyps has been emphasized frequently since a fair percentage of those treated will later be found to have recurrent polyps or frank malignancy.[4] Having examined many patients by coloscopy to find numerous polyps not demonstrated on repeated barium studies, we are convinced and have convinced our roentgenologist of the shortcomings of roentgenologic demonstration of polyps. However, we have not as yet felt justified in recommending repeat laparotomy and coloscopy as a follow-up study when barium studies and clinical findings are negative.

SUMMARY

A technic of examining the entire colonic mucosa by means of coloscopy using a sterile sigmoidoscope at the time of exploratory laparotomy is described.

This is the only method of accurately determining the number of polyps present since roentgenographic studies are probably not more than 50 per cent accurate.

With thorough bowel preparation and careful technic the hazards of this method are minimal.

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EDITORIAL

HAS CURARE BEEN MALIGNED?

With the introduction of the "*curare*" drugs as muscle relaxants in the speciality of anesthesiology and the practice of surgery by Griffith in 1942, numerous studies have appeared in the literature reporting on the efficacy of curare in facilitating operations by providing the maximum of relaxation. With the relaxation provided by the "*curare*" drugs, surgeons have been able to obtain quiescence and increase exposure without the use of numerous packs within the abdomen. In addition, the anesthesiologists have been able to use a lighter plane of surgical anesthesia which maintains a more normal physiologic state than deep surgical anesthesia. Deep surgical anesthesia requires a maximum concentration of anesthetic agents which produce by themselves deleterious effects upon the circulation and respiration. The aftermath of this "*physiologic imbalance*" has frequently been manifested in the increased postoperative morbidity of the patient.

With the advent of curare, the anesthesiologist has been able to provide better anesthesia and smoother working conditions for the surgeon. This has been reflected in the patient by a smoother and a more complacent postoperative recovery.

Recently, a report by Beecher and Todd questions the validity for using curare. In fact, they are of the opinion that a threefold increase in postoperative deaths has occurred since "*curare*" has been used. Statistically they have shown this to be true. However, they equivocate in stating that this may not be true if ideal test situations could be analyzed. In other words, a comparable number of cases of patients having the same operative procedures with and without the use of a "*curare*" agent has not been studied. Even such a study, to be valid, would have to be in the same sex, age, and physical status groups, with the same surgeon and anesthesiologist. Such a study would answer the question unequivocally.

Lorhan and Chen reviewed the cases of 563 patients who had cholecystectomies of whom 440 received a curare agent. This series of cases was compared with one studied by Orr in 1947 which consisted of 558 cases. The over-all mortality rate in 563 cases was 1.77 per cent, as compared to 2.8 per cent in 558. If we were to include the 123 patients who did not receive a curarizing agent with the 558 cases in Orr's series, the mortality rate would be 2.5 per cent, as compared to 2.05 per cent in 440 patients who received a curare drug. Therefore, if, as Beecher contends, curare increases the mortality rate, an increase should have been seen in our series.

It is difficult to envision all deaths following surgery as the result of anesthesia. Surgery itself, carries with it an inherent mortality rate. The assumption that curare is the causative factor is erroneous. The condemnation of an agent such as curare, therefore, is without merit. It is true that ether is the most frequently used agent, and a number of deaths have followed the use of this agent. Why not then say that all deaths following ether anesthesia are due to "*ether*"?

Curare is not an innocuous agent, nor should it be used indiscriminately or

by the unskilled. Curare is a very potent respiratory depressant, and patients may frequently become overdosed if it is used injudiciously. Curare is not to be used to supplant good surgical anesthesia, but is an aid to good and better anesthesia. Curare will mask a bad anesthetic and allow the anesthesiologist to meet all the requirements for a good anesthetic. The use of a curare as a masking agent for a bad anesthetic is to be condemned.

All too frequently, anesthetic agents or drugs have been condemned as the responsible factor in the cause of death. Rather than persist in stating this philosophy, surgeons and anesthesiologists should become cognizant of the fact that they as individuals may be the principal offenders.

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BOOKS RECEIVED

Books received are acknowledged in this section, and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

Suprapubic Prostatectomy with Primary Closure of the Bladder by an Original Method. By Univ. Prof. Dr. Theodor Hryntschak, Late Director, Urologischen Abteilung der Wiener Stadtischen Allgemeinen Poliklinik. Authorized translation by Noble S. R. Maluf, M.S., M.D., Ph.D., Chief of Urology, Surgical Service, Veterans Administration Hospital, Houston, Texas, Assistant Professor of Urology, Baylor University College of Medicine. Charles C Thomas, Publisher, Springfield, Illinois. Revised 1955. Price $8.50.

Introduction to Operating-Room Technique. By Edna Cornelia Berry, R.B., A.B., Head Nurse, Operating Rooms, University Hospitals of Cleveland, Cleveland, Ohio and Mary Louise Kohn, A.B., R.N., M.N., Formerly Instructor in Operating-Room Technique, Frances Payne Bolton School of Nursing, Western Reserve University, Cleveland, Ohio. Blakiston Division, McGraw-Hill Book Company, Inc., New York, Toronto, London. 1955. Price $4.00.

Atlas of Rush Pin Technics, A System of Fracture Treatment. By Leslie V. Rush, M.D., F.A.C.S., F.I.C.S., Department of Surgery, Rush Memorial Hospital, Meridian, Mississippi. The Berivon Company, Meridian, Mississippi, 1955.

Salivary Gland Tumors. By Donald E. Ross, M.D., F.A.C.S., F.I.C.S., F.R.C.S. (Eng.) F.R.C.S. (Edin.); Diplomate, The American Board of Surgery; Chief Surgeon, Ross-Loos Medical Group, Los Angeles, California. Charles C Thomas, Publisher, Springfield, Illinois. 1955. Price $7.50.

Office Procedures. By Paul Williamson, M.D., W. B. Saunders Company, Philadelphia and London, 1955. Price $12.50.

Basic Surgical Skills. A Manual with Appropriate Exercises. By Robert Tauber, M.D., F.A.C.S., Assistant Professor of Gynecology and Obstetrics, Graduate School of Medicine, University of Pennsylvania. Illustrated. W. B. Saunders Company, Philadelphia and London, 1955. Price $3.75.

Understanding Surgery. By R. E. Rothenberg, M.D., Editor. Pocket Books, Inc., New York. 1955. Price $0.50.

New Concepts in Surgery of the Vascular System. By Emile Holman, M.D., Professor of Surgery, Stanford University School of Medicine. Publication Number 271, American Lecture Series. Charles C Thomas, Publisher, Springfield, Illinois. 1955.